



THE TRACT
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The
Neurology Tract
A board review for the FEBN

Eighteen chapters of high-yield neurology, revised against the guidelines and trials current in 2026.

Pattern recognition

Current diagnostic criteria

Landmark trials

Radiological signs

Emergency protocols

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About this edition

TITLE	<i>The Neurology Tract</i> — 2026 edition, corrected and updated
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PURPOSE	Revision companion for the European Board of Neurology examination (FEBN), closed-book and open-book components
SOURCES	<i>Merritt's Neurology</i> , <i>Adams and Victor's Principles of Neurology</i> , <i>Bradley and Daroff's Neurology in Clinical Practice</i> , <i>Aminoff's Neurology and General Medicine</i> ; current EAN, AAN, AHA/ASA, ILAE, MDS, ICHD-3, ICSD-3 and WHO CNS5 publications and primary trial reports
THIS EDITION	Every chapter re-checked; factual corrections and guideline updates are listed in “What changed in the 2026 edition”
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Also by the author: *The Book of Seizures* (doi:10.5281/zenodo.23140760) · *Najm Neurocritical Guide* (doi:10.5281/zenodo.23212899).

Contents

1	Neurological Examination and Neuroanatomy	5
2	Vascular Neurology (Stroke)	10
3	Epilepsy	14
4	Movement Disorders	18
5	Multiple Sclerosis and Demyelinating Diseases	23
6	Neuromuscular Disorders	27
7	Headache and Facial Pain	32
8	Infections of the Nervous System	36
9	Neuro-oncology	41
10	Dementia and Cognitive Disorders	45
11	Sleep Disorders	49
12	Autonomic Disorders	52
13	Neuro-ophthalmology and Neuro-otology	54
14	Neurological Complications of Systemic Disease	57
15	Paediatric Neurology Essentials	60
16	Neurogenetics	63
17	Ethics, Coma and Brain Death	66
18	Quick Reference and Emergency Protocols	69

Preface and how to use this guide

The Neurology Tract is a companion for the European Board of Neurology examination (FEBN). It distils the standard references — *Merritt's Neurology*, *Adams and Victor's Principles of Neurology*, *Bradley and Daroff's Neurology in Clinical Practice* and *Aminoff's Neurology and General Medicine* — into a board-focused format, and brings each topic up to the guideline editions current in 2026.

How this guide is built

- **Pattern-recognition tables** close every chapter — the radiological and clinical signs that image-based questions are written around.
- **Evidence boxes** summarise the trials that changed practice, with the numbers that examiners ask for.
- **Diagnostic criteria** are given in their current edition: McDonald 2017 (with the 2024 revision noted), McKeith 2017, ICHD-3, EAN/PNS 2021, WHO CNS5 2021, ICSD-3.
- **Emergency protocols** and quick-reference tables sit in Chapter 18 for the last week before the exam.

Study plan. First pass: read the chapters in order. Second pass: tables, boxes and pattern-recognition sections only. Final week: Chapter 18 and the evidence boxes.

About the examination. The FEBN has a closed-book multiple-choice component and an open-book, case-based component. Pattern recognition, evidence-based practice and clinical reasoning run through both, so the radiological signs and trial summaries in this guide are written to be usable in either.

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What changed in the 2026 edition

Every chapter was re-checked against current guidelines and primary trial reports. The changes that matter for the examination:

Chapter	2025 edition said	2026 edition says
2 Stroke	ICH score 30-day mortality 0 = 13 %, 1 = 26 %, 2 = 72 %	Shifted one point: 0 = 0 %, 1 = 13 %, 2 = 26 %, 3 = 72 %, 4 = 97 %, 5 = 100 % (Hemphill 2001)
2 Stroke	Triple-H therapy for vasospasm	Euvolaemia plus induced hypertension; hypervolaemia and haemodilution are no longer recommended
2 Stroke	CHANCE-2: "7.6 % vs 6.0 %", no excess bleeding	Ticagrelor-aspirin 6.0 % vs clopidogrel-aspirin 7.6 %; more total (not severe) bleeding with ticagrelor
2 Stroke	Thrombectomy for ASPECTS ≥ 6 only	Large-core trials (SELECT2, ANGEL-ASPECT, RESCUE-Japan LIMIT) added
2 Stroke	"Fern-like pattern" for amyloid angiopathy	Cortical superficial siderosis and convexity SAH on SWI
3 Epilepsy	Epilepsy = more than two seizures	Two or more unprovoked seizures > 24 h apart (ILAE 2014)
3 Epilepsy	Lamotrigine for JME; first-line in absence	Lamotrigine may worsen myoclonus; inferior to ethosuximide and valproate in absence (Glauser 2010)
3 Epilepsy	DBS "under investigation"	ANT-DBS approved (EU 2010, FDA 2018; SANTE)
3 Epilepsy	Old syndrome names	ILAE 2022 names (SeLECTS, SeLEAS, COVE)
4 Movement	Dystonia: early < 26 / late > 26 y; HD normal < 26 repeats	2013 consensus age bands; HD normal ≤ 26 repeats
4 Movement	UK Brain Bank only; MAO-B "disease-modifying"	MDS 2015 criteria added; no proven disease modification
5 MS	McDonald 2017 without CSF bands; PRMS listed	CSF-specific oligoclonal bands substitute for DIT; PRMS retired (Lublin 2013); 2024 revision noted
5 MS	"Turnbull's blue" as an MRI sign	Removed — Turnbull's blue is an iron stain. T1 black holes and paramagnetic rim lesions instead
6 Neuromuscular	GBS intubation at FVC < 15 mL/kg; edrophonium test	20/30/40 rule; ice-pack test (edrophonium obsolete); thymectomy per MGTX; new complement and FcRn drugs
6 Neuromuscular	EI Escorial; "definite CIDP"; Popeye = distal biceps	Gold Coast 2020; EAN/PNS 2021 has no "definite" tier; Popeye = proximal (long-head) rupture, also FSHD
7 Headache	Erenumab 56 % responders at 70 mg; SUNCT ≥ 3 /day	STRIVE: 43 % (70 mg) and 50 % (140 mg); SUNCT at least once daily
8 Infection	PLEDs; CJD survival 6 months	LPDs (ACNS 2021); median survival ~4–6 months; RT-QulC as key test
8 Infection	IV ceftriaxone for all CNS Lyme	Oral doxycycline adequate for meningitis, cranial neuritis and radiculitis
9 Oncology	WHO 2016 grading ("anaplastic", "secondary GBM")	WHO CNS5 2021 — glioblastoma is IDH-wildtype by definition
9 Oncology	"Snowball" sign for lymphoma	Snowball lesions belong to Susac syndrome; lymphoma signs corrected
10 Dementia	Aducanumab listed; "possible DLB" from supportive features	Aducanumab withdrawn 2024, donanemab added; McKeith 2017 possible-DLB rule corrected
10 Dementia	FTD the commonest dementia under 65	Alzheimer's remains commonest under 65; FTD is second
11 Sleep	Narcolepsy MSLT < 8 min; no NT1/NT2	ICSD-3: NT1/NT2, MSLT ≤ 8 min + ≥ 2 SOREMPs, hypocretin ≤ 110 pg/mL; pitolisant and solriamfetol added
11 Sleep	Dopamine agonists first-line for RLS	AASM 2024: iron and $\alpha 2\delta$ ligands first; standard use of dopamine agonists not recommended

Chapter	2025 edition said	2026 edition says
13 Neuro-otology	Hearing loss implies a peripheral cause	AICA infarction can cause acute hearing loss with vertigo (HINTS-plus)
13 Neuro-ophthalmology	Vestibular schwannoma "with dural tail"	Dural tail favours meningioma; schwannoma extends into the internal auditory canal
15 Paediatrics	ENDEAR as the gene-therapy trial	ENDEAR tested nusinersen; onasemnogene was START (2017)
17 Brain death	$\text{PaCO}_2 \geq 60$ or rise ≥ 20 mmHg; EEG as a confirmatory test; US law	$\text{pH} < 7.30$ and $\text{PaCO}_2 \geq 60$ and ≥ 20 above baseline; ancillary tests are blood-flow studies (2023 consensus); criteria follow national law
18 Quick reference	Vancomycin in every adult meningitis regimen; CSF pressure 7–18 cmH ₂ O	Vancomycin only where pneumococcal resistance is common (European practice); 10–20 cmH ₂ O (to 25 in obesity)
18 Trials	"CONFIRM (2010)" for dabigatran	RE-LY (2009)

Neurological Examination and Neuroanatomy

Key tables: Mental status examination · MMSE · Cranial nerves · MRC grading · Spinal cord syndromes · Brainstem syndromes

The neurological examination is the instrument of localisation: its purpose is to decide where in the nervous system the problem lies, and only then what it is.

Purpose	Systematic assessment of nervous system function to localise lesions and guide diagnosis
Components	Mental status, cranial nerves, motor, sensory, coordination, gait, reflexes
Key principle	Localisation before aetiology
Documentation	Clear, systematic recording of normal and abnormal findings

Mental status examination

Domain	Assessment
Level of consciousness	Alertness, attention, responsiveness (GCS if impaired)
Orientation	Person, place, time, situation
Attention	Digit span (forward 7 ± 2 , backward 5 ± 2), months backward
Language	Spontaneous speech, comprehension, repetition, naming, reading, writing
Memory	Immediate (3 words), recent (current events), remote
Visuospatial	Clock drawing, intersecting pentagons, figure copying
Executive function	Trail Making Test, verbal fluency (FAS), abstraction
Praxis	Use of objects, sequential tasks
Neglect	Line bisection, double simultaneous stimulation

MMSE. A 30-point screen. 24–30 normal, 18–23 mild impairment, 0–17 severe impairment. Domains: orientation 10 (time 5, place 5), registration 3, attention/calculation 5 (serial 7s or WORLD backwards), recall 3, language 9 (naming, repetition, three-step command, reading, writing), visuospatial 1 (pentagons). Scores are education-dependent.

MoCA. A 30-point test, more sensitive than the MMSE for mild cognitive impairment because it adds executive and attentional tasks. Normal ≥ 26 (add one point if ≤ 12 years of education).

Cranial nerves

Nerve	What to test	Points that are examined
I Olfactory	Non-irritant odours (coffee, vanilla, clove)	Anosmia: trauma, frontal tumour, Parkinson's, COVID-19. Ammonia tests the trigeminal nerve, not smell
II Optic	Acuity, fields, fundi, pupillary reflexes	Swinging-light test for RAPD
III, IV, VI	Pursuit in an H pattern, pupils, ptosis, nystagmus	Complete ptosis = III; partial ptosis = Horner's or myasthenia
V Trigeminal	Sensation V1–V3, corneal reflex, masseter/temporalis	Corneal reflex: afferent V1, efferent VII
VII Facial	Symmetry, forehead, eye closure, smile, taste (anterior $\frac{2}{3}$)	Forehead spared in UMN lesions, involved in LMN lesions

Nerve	What to test	Points that are examined
VIII	Whisper, Weber and Rinne; head impulse, Dix–Hallpike	
IX, X	Palate, gag, voice, swallow	Uvula deviates away from the side of the lesion. Gag: afferent IX, efferent X
XI	Sternocleidomastoid and trapezius	
XII	Tongue at rest and protruded	Fasciculation and atrophy in ALS; protrusion deviates towards a LMN lesion

Motor examination

Bulk. Atrophy (focal or diffuse), fasciculations (ALS, radiculopathy), hypertrophy or pseudohypertrophy (dystrophies, myotonia congenita).

Tone	Description	Cause
Spasticity	Velocity-dependent, clasp-knife	UMN lesion
Rigidity	Velocity-independent, lead-pipe; cogwheel when tremor is superimposed	Parkinsonism
Paratonia (gegenhalten)	Resistance that varies with the examiner's movement	Frontal lobe dysfunction
Hypotonia	Reduced tone	LMN, cerebellar, acute spinal shock
Dystonia	Sustained abnormal posture	Basal ganglia

MRC grade	Description
5	Normal
4+ / 4 / 4–	Movement against strong / moderate / slight resistance
3	Against gravity, no resistance
2	With gravity eliminated
1	Flicker or trace contraction
0	None

Pattern	Localisation	Example
Hemiparesis	Contralateral cortex or internal capsule	Stroke
Paraparesis	Bilateral corticospinal tracts (thoracic cord) or parasagittal lesion	Cord compression, parasagittal meningioma
Quadriparesis	Cervical cord, brainstem, diffuse peripheral	GBS, ALS, myasthenia
Proximal	Muscle or neuromuscular junction	Myopathy, MG
Distal	Peripheral nerve or anterior horn cell	Length-dependent neuropathy, ALS
Monoparesis	Nerve, root or plexus (or small cortical lesion)	Radial nerve palsy

Sensory examination

Modality	Pathway	Test
Light touch	Dorsal column and spinothalamic	Cotton wisp
Pain	Spinothalamic	Pin
Temperature	Spinothalamic	Cold tuning fork
Vibration	Dorsal column	128 Hz tuning fork

Modality	Pathway	Test
Joint position	Dorsal column	Distal phalanx
Two-point discrimination	Cortical	Calibrated compass

Pattern	Description	Localisation
Stocking-glove	Distal, symmetric, length-dependent	Polyneuropathy
Dermatomal	Root distribution	Radiculopathy
Hemisensory	Face, arm and leg on one side	Contralateral thalamus or cortex
Sensory level	Loss below a level	Spinal cord
Dissociated	Pain/temperature lost, vibration kept (or the reverse)	Syringomyelia, Brown-Séquard, anterior cord
Cortical	Astereognosis, agraphesthesia, extinction	Parietal cortex

Coordination and gait

Cerebellar testing: finger–nose (dysmetria, intention tremor), heel–shin, rapid alternating movements (dysdiadochokinesia), rebound.

Gait	Description	Localisation
Hemiplegic	Circumduction, flexed arm	Contralateral corticospinal tract
Spastic	Scissoring, toe-walking	Bilateral corticospinal tracts
Steppage	Foot drop, high stepping	Common peroneal nerve, L5 root
Ataxic	Wide-based, veering	Cerebellum or vestibular system
Sensory ataxic	Watches feet, worse with eyes closed (Romberg positive)	Dorsal columns, large-fibre neuropathy
Parkinsonian	Shuffling, festination, reduced arm swing	Basal ganglia
Magnetic	Feet "stuck", start hesitation	Normal-pressure hydrocephalus, frontal disease
Waddling	Trendelenburg bilaterally	Proximal myopathy

Reflexes

Reflex	Root	Muscle
Biceps	C5–C6	Biceps brachii
Brachioradialis	C5–C6	Brachioradialis
Triceps	C7–C8	Triceps
Knee	L3–L4	Quadriceps
Ankle	S1–S2	Gastrocnemius–soleus

Grading: 0 absent, 1+ reduced, 2+ normal, 3+ brisk, 4+ clonus.

Sign	Meaning
Babinski (extensor plantar)	UMN lesion
Hoffmann	Corticospinal tract lesion above C5–C6 (also seen in some normal people)
Brisk jaw jerk	Bilateral UMN lesion above the pons (pseudobulbar palsy)
Snout, palmomental, glabellar	Frontal release signs; non-specific

Essential neuroanatomy

Area	Function	Lesion
Precentral gyrus	Voluntary movement	Contralateral weakness
Postcentral gyrus	Somatosensation	Contralateral cortical sensory loss
Broca's area (BA 44, 45)	Speech production	Non-fluent aphasia
Wernicke's area (posterior BA 22)	Comprehension	Fluent aphasia
Dominant angular gyrus	Reading, calculation	Gerstmann syndrome (agraphia, acalculia, finger agnosia, left-right confusion)
Primary visual cortex (BA 17)	Vision	Contralateral homonymous hemianopia, often macular-sparing
Frontal eye field (BA 8)	Contralateral saccades	Destructive lesion: eyes look towards the lesion. Irritative (seizure): eyes turn away

Spinal cord syndromes

Syndrome	Findings	Causes
Complete transection	Bilateral motor, sensory and autonomic loss below the level	Trauma, tumour, transverse myelitis
Central cord	Arms weaker than legs, sacral sparing	Hyperextension injury, syrinx
Brown-Séquard	Ipsilateral weakness and dorsal-column loss; contralateral pain/temperature loss	Penetrating injury, MS
Anterior cord	Bilateral weakness and pain/temperature loss; vibration and proprioception spared	Anterior spinal artery infarction
Posterior cord	Loss of vibration and proprioception, sensory ataxia	B12 or copper deficiency, tabes dorsalis
Conus medullaris	Saddle anaesthesia, early sphincter failure, symmetric, mixed UMN/LMN	Tumour, disc
Cauda equina	Asymmetric radicular pain and weakness, later sphincter failure, LMN	Disc herniation, tumour

Brainstem syndromes

Syndrome	Findings	Site
Weber	Ipsilateral III palsy + contralateral hemiparesis	Ventral midbrain (cerebral peduncle)
Benedikt	Ipsilateral III palsy + contralateral tremor or choreoathetosis	Midbrain tegmentum, red nucleus
Millard-Gubler	Ipsilateral VI and VII palsy + contralateral hemiparesis	Ventral pons
Wallenberg	Vertigo, nystagmus, dysphagia, hoarseness, ipsilateral facial and contralateral body pain/temperature loss, ipsilateral Horner's and ataxia	Lateral medulla (vertebral artery or PICA)
Dejerine (medial medullary)	Ipsilateral XII palsy, contralateral hemiparesis and dorsal-column loss	Medial medulla (anterior spinal artery)

Pattern recognition — Chapter 1

Sign	Description	Condition
Dawson's fingers	Ovoid lesions perpendicular to the lateral ventricles	Multiple sclerosis

Sign	Description	Condition
Pulvinar (hockey-stick) sign	Bilateral posterior and dorsomedial thalamic hyperintensity on FLAIR/DWI	Variant CJD
Eye-of-the-tiger	Pallidal T2 hypointensity with a central hyperintense spot	PKAN (PANK2)

Vascular Neurology (Stroke)

Key tables: BE-FAST · Time windows for reperfusion · ICH score · Hunt and Hess · ABCD2

Definition	Acute focal neurological deficit of vascular cause, with infarction or haemorrhage
Types	Ischaemic ~85 %, haemorrhagic ~15 % (ICH 10–15 %, SAH ~5 %)
Burden	A leading cause of death and the leading cause of acquired adult disability
Principle	Time is brain — roughly 1.9 million neurons are lost each minute of untreated large-vessel occlusion

Ischaemic stroke

Thrombosis, embolism or hypoperfusion start an ischaemic cascade of excitotoxicity, calcium overload and free-radical injury. The salvageable penumbra is the target of every acute treatment.

TOAST subtype	Frequency	Mechanism
Large-artery atherosclerosis	15–20 %	Stenosis or occlusion of a major artery
Cardioembolism	20–25 %	Atrial fibrillation, valve disease, cardiomyopathy
Small-vessel occlusion (lacunar)	~25 %	Lipohyalinosis of penetrating arteries
Other determined cause	~5 %	Dissection, vasculitis, thrombophilia
Undetermined	30–40 %	Cryptogenic, two causes, or incomplete work-up

Territory	Artery	Features
Anterior	MCA	Contralateral face/arm > leg weakness and sensory loss; aphasia (dominant) or neglect (non-dominant); hemianopia
Anterior	ACA	Contralateral leg > arm weakness, abulia, urinary incontinence
Posterior	PCA	Homonymous hemianopia, alexia without agraphia (dominant), memory loss, thalamic syndromes
Posterior	Basilar	Quadriparesis, locked-in syndrome, coma, cranial nerve palsies
Posterior	Vertebral/PICA	Lateral medullary (Wallenberg) syndrome
Lacunar	Penetrators	Pure motor, pure sensory, sensorimotor, ataxic hemiparesis, dysarthria–clumsy hand

BE-FAST: Balance, Eyes (visual loss or diplopia), Face, Arm, Speech, Time.

Acute management

Window	Intervention	Key selection criteria
0–4.5 h	IV thrombolysis — alteplase 0.9 mg/kg or tenecteplase 0.25 mg/kg	Disabling deficit, no haemorrhage, no contraindication
Unknown onset / wake-up	IV thrombolysis guided by imaging	DWI–FLAIR mismatch (WAKE-UP) or perfusion mismatch (EXTEND)
0–6 h	Mechanical thrombectomy	Anterior LVO (ICA, M1), ASPECTS ≥ 6, pre-stroke mRS 0–1
0–24 h, large core	Thrombectomy	ASPECTS 3–5 or large core on perfusion (SELECT2, ANGEL-ASPECT, RESCUE-Japan LIMIT, 2022–23)
6–24 h	Thrombectomy	Clinical–core or perfusion mismatch (DAWN, DEFUSE-3)
0–24 h, basilar	Thrombectomy	Moderate–severe basilar occlusion (ATTENTION, BAOCHE, 2022)

Evidence – DAWN and DEFUSE-3 (2018). Thrombectomy up to 24 h in patients with clinical–imaging mismatch. Functional independence (mRS 0–2) at 90 days: DAWN 49 % vs 13 %; DEFUSE-3 45 % vs 17 %. Imaging selection replaced the clock.

NIHSS. 0–42. 0 none, 1–4 minor, 5–15 moderate, 16–20 moderate–severe, 21–42 severe.

Main contraindications to thrombolysis. Intracranial haemorrhage on imaging; ischaemic stroke, serious head trauma or intracranial/spinal surgery within 3 months; intracranial neoplasm, AVM or unsecured aneurysm; active internal bleeding or GI bleeding within 21 days; platelets $< 100 \times 10^9/L$, INR > 1.7 , aPTT > 40 s, or a therapeutic-dose DOAC within 48 h without normal specific testing; BP that cannot be brought below 185/110 mmHg.

Secondary prevention

Scenario	Recommendation
Non-cardioembolic stroke or TIA	Aspirin 75–100 mg or clopidogrel 75 mg
Minor stroke (NIHSS ≤ 3) or high-risk TIA (ABCD2 ≥ 4)	Aspirin + clopidogrel for 21 days, started within 24 h, then single agent (CHANCE, POINT)
Symptomatic intracranial stenosis 70–99 %	Aspirin + clopidogrel for 90 days, intensive risk-factor control (SAMMPRIS)

Evidence – CHANCE-2 (2021). In minor stroke or TIA with *CYP2C19* loss-of-function alleles, 90-day stroke recurrence was 6.0 % with ticagrelor + aspirin versus 7.6 % with clopidogrel + aspirin. Severe or moderate bleeding did not differ; total bleeding was higher with ticagrelor (5.3 % vs 2.5 %).

Condition	Anticoagulation
Atrial fibrillation	DOAC preferred over warfarin (apixaban, rivaroxaban, dabigatran, edoxaban)
Mechanical valve	Warfarin — INR 2.0–3.0 (aortic) or 2.5–3.5 (mitral). DOACs contraindicated
Rheumatic mitral stenosis with AF	Warfarin, INR 2.0–3.0 (INVICTUS: DOAC inferior)

Risk factor	Target
Blood pressure	$< 130/80$ mmHg after the acute phase
LDL cholesterol	< 70 mg/dL (1.8 mmol/L) with high-intensity statin $\pm$ ezetimibe (TST trial)
Diabetes	HbA1c < 7 %
Smoking	Cessation
Activity	≥ 150 min/week moderate exercise

Intracerebral haemorrhage

ICH causes 10–15 % of strokes but about 40 % die within a month. Hypertensive sites: putamen/basal ganglia (most common), thalamus, pons, cerebellum.

Cause	Characteristics
Hypertension	Deep: basal ganglia, thalamus, pons, cerebellum
Cerebral amyloid angiopathy	Lobar haemorrhage in the elderly, lobar microbleeds, cortical superficial siderosis (Boston criteria 2.0)
Anticoagulation	Larger volumes and more expansion
Vascular malformation	AVM, cavernoma, dural AV fistula
Coagulopathy	Thrombocytopenia, haemophilia, liver disease

Cause	Characteristics
Tumour	Melanoma, renal cell, choriocarcinoma, thyroid metastases; glioblastoma
Drugs	Cocaine, amphetamines

ICH score component	Points
GCS 3–4 / 5–12 / 13–15	2 / 1 / 0
Volume ≥ 30 mL	1
Intraventricular extension	1
Infratentorial origin	1
Age ≥ 80 years	1

30-day mortality (Hemphill 2001): 0 points 0 %, 1 point 13 %, 2 points 26 %, 3 points 72 %, 4 points 97 %, 5 points 100 %. The score estimates risk; it should not be used to limit care on day one.

Management.

- Blood pressure: lower systolic to about 140 mmHg (130–150) within an hour and keep it stable; avoid < 130 mmHg and large drops (INTERACT2, ATACH-2, INTERACT3 care bundle).
- Reverse anticoagulation at once: four-factor PCC + vitamin K for warfarin; idarucizumab for dabigatran; andexanet alfa (ANNEXA-I) or PCC for factor Xa inhibitors.
- Surgery: cerebellar haemorrhage > 3 cm or with brainstem compression or hydrocephalus. Minimally invasive evacuation of lobar haematomas 30–80 mL is supported by ENRICH (2024).
- Raised ICP: head up 30°, osmotherapy, EVD for hydrocephalus.
- Seizures: no prophylaxis; treat seizures if they occur.

Subarachnoid haemorrhage

About 85 % of non-traumatic SAH is aneurysmal. Thunderclap headache reaches maximum within a minute. CT is ~100 % sensitive within 6 h of onset; after that, LP for xanthochromia.

Hunt and Hess	Description	Approximate mortality
I	Asymptomatic or mild headache, slight neck stiffness	~10 %
II	Moderate–severe headache, neck stiffness, no deficit except cranial nerve palsy	~25 %
III	Drowsy or confused, mild focal deficit	~40 %
IV	Stupor, moderate–severe hemiparesis	~70 %
V	Coma, extensor posturing	~100 %

The WFNS scale (GCS-based) is used more often in current trials.

Management.

- Secure the aneurysm early (within 24–72 h). Coiling where both options are suitable (ISAT); clipping for some MCA aneurysms and haematoma requiring evacuation.
- Nimodipine 60 mg orally every 4 h for 21 days – improves outcome; the effect is not through angiographic vasospasm.
- Watch for delayed cerebral ischaemia days 3–14: clinical examination, TCD, CT perfusion.
- Maintain euvolaemia. For symptomatic DCI, induce hypertension and consider endovascular therapy. **Prophylactic hypervolaemia, haemodilution and "triple-H therapy" are no longer recommended** (AHA/ASA 2023, NCS).
- EVD for acute hydrocephalus. Treat hyponatraemia with fluid and salt, not fluid restriction.

Transient ischaemic attack

TIA is a transient episode of focal brain, spinal cord or retinal ischaemia **without acute infarction** (tissue-based definition). The 24-hour rule is obsolete.

ABCD2	Points
Age $\geq$ 60	1
BP $\geq$ 140/90 at first assessment	1
Unilateral weakness / speech disturbance without weakness	2 / 1
Duration $\geq$ 60 min / 10–59 min	2 / 1
Diabetes	1

2-day stroke risk: 0–3 points 1.0 %, 4–5 points 4.1 %, 6–7 points 8.1 %. Modern pathways treat all TIAs as urgent regardless of score.

Work-up. Assessment within 24 h; MRI with DWI (positive in ~30 %); CTA or MRA of head and neck; ECG and prolonged rhythm monitoring for paroxysmal AF; immediate antiplatelet therapy; risk-factor control.

Cervical artery dissection

A leading cause of stroke under 50. Unilateral head or neck pain, partial Horner's syndrome (ptosis and miosis; anhidrosis is usually absent with internal carotid dissection), pulsatile tinnitus, lower cranial nerve palsies, and ischaemia hours to days after the pain. May follow minor trauma.

- Imaging: CTA or MRA with fat-saturated T1 (crescentic intramural haematoma); catheter angiography if doubt remains.
- Treatment: antiplatelet or anticoagulant therapy for 3–6 months — neither proven superior (CADISS 2015, TREAT-CAD 2021). Stenting for recurrent ischaemia despite medical therapy.

Pattern recognition — Chapter 2

Sign	Description	Condition
Hyperdense MCA sign	Hyperdense MCA on non-contrast CT	Acute MCA thrombus
MCA dot sign	Hyperdense dot in the Sylvian fissure	M2/M3 branch thrombus
Insular ribbon sign	Loss of grey–white differentiation in the insula	Early MCA ischaemia
CTA spot sign	Contrast extravasation within a haematoma	Active bleeding; predicts expansion
Swirl sign	Hypodense swirls within a hyperdense haematoma	Active bleeding (also extradural haematoma)
Cortical superficial siderosis	Gyriform hypointensity along cortical surfaces on SWI/GRE	Cerebral amyloid angiopathy (also convexity SAH)
String-of-beads	Alternating stenosis and dilatation on angiography	Fibromuscular dysplasia; also RCVS

Epilepsy

Key tables: ILAE 2017 seizure classification · Syndromes (ILAE 2022) · Drug choice by seizure type · Status epilepticus · Surgery and neuromodulation

Definition (ILAE 2014)	Two unprovoked seizures > 24 h apart; or one unprovoked seizure with recurrence risk $\geq$ 60 %; or an epilepsy syndrome
Prevalence	~0.7–1 % (about 50 million people worldwide)
Incidence	Bimodal: highest under 2 years and over 65
Aetiology	Structural, genetic, infectious, metabolic, immune, unknown

Seizure classification (ILAE 2017)

Onset	Description	Examples
Focal	Arises within one hemisphere	Focal aware, focal impaired awareness, focal to bilateral tonic-clonic
Generalised	Engages bilateral networks from onset	Absence, myoclonic, tonic, atonic, tonic-clonic
Unknown	Onset not determined	Tonic-clonic of unknown onset, epileptic spasms

Focal seizure	Awareness	Notes
Focal aware	Preserved	Motor, sensory, autonomic, cognitive or emotional features (old "simple partial")
Focal impaired awareness	Impaired	Often automatisms (old "complex partial")
Focal to bilateral tonic-clonic	—	Old "secondarily generalised"

Generalised seizure	Characteristics
Typical absence	Seconds of unresponsiveness, no post-ictal state, 3 Hz spike-wave, provoked by hyperventilation
Myoclonic	Brief shock-like jerks, often on waking
Tonic	Sustained stiffening, often in sleep
Atonic	Sudden loss of tone — drop attacks
Tonic-clonic	Tonic then clonic phase, post-ictal confusion

Lobe	Semiology
Temporal (mesial)	Rising epigastric sensation, déjà vu, fear, olfactory or gustatory aura; behavioural arrest, orolimentary and manual automatisms; contralateral dystonic posturing; post-ictal confusion
Frontal	Brief, nocturnal, clustered; hypermotor activity, vocalisation, asymmetric tonic posturing (SMA); little post-ictal confusion
Parietal	Sensory symptoms (tingling, numbness, pain), vertigo, visual illusions
Occipital	Elementary coloured visual hallucinations, visual loss, eye deviation, forced blinking

Epilepsy syndromes (ILAE 2022 nomenclature)

Syndrome	Age	Features	Treatment
Childhood absence epilepsy	4–10 y	Many daily absences, 3 Hz spike-wave, normal development	Ethosuximide (absence only); valproate if GTCS coexist

Syndrome	Age	Features	Treatment
Self-limited epilepsy with centrotemporal spikes (SeLECTS; formerly BECTS)	4–10 y	Nocturnal hemifacial motor seizures, drooling, speech arrest; centrotemporal spikes activated by sleep	Often none; if needed levetiracetam or oxcarbazepine/carbamazepine
Self-limited epilepsy with autonomic seizures (SeLEAS; formerly Panayiotopoulos)	3–6 y	Prolonged autonomic seizures with vomiting, pallor, eye deviation	Usually none
Childhood occipital visual epilepsy (COVE; formerly Gastaut)	8–9 y	Brief elementary visual seizures, post-ictal headache	Carbamazepine or oxcarbazepine
Lennox–Gastaut syndrome	3–5 y	Tonic seizures in sleep, atonic drops, atypical absence; slow spike-wave < 2.5 Hz; intellectual disability	Valproate, lamotrigine, rufinamide, clobazam, cannabidiol, fenfluramine; ketogenic diet; callosotomy
Dravet syndrome	< 1 y	Prolonged febrile hemiclonic seizures, then multiple types; <i>SCN1A</i> loss of function	Valproate, clobazam, stiripentol, fenfluramine, cannabidiol. Avoid sodium-channel blockers
Juvenile myoclonic epilepsy	12–18 y	Morning myoclonus, GTCS, absences in a third; 4–6 Hz polyspike-wave, photosensitivity	Valproate (most effective); levetiracetam in women of childbearing potential. Lamotrigine may worsen myoclonus
Juvenile absence epilepsy	10–17 y	Fewer absences than CAE, GTCS common	Valproate; levetiracetam or lamotrigine as alternatives
Mesial temporal lobe epilepsy with hippocampal sclerosis	Any	Focal impaired awareness seizures with aura; often drug-resistant	Anterior temporal lobectomy

Investigation

EEG. A routine 20–30 min EEG shows interictal discharges in about half of people with epilepsy; repeat and sleep-deprived recordings raise the yield. Video-EEG captures events for classification and pre-surgical localisation; ambulatory EEG for infrequent events. A normal EEG does not exclude epilepsy.

Imaging. Epilepsy-protocol MRI for every adult with new seizures: 3D T1, T2, FLAIR, DWI, SWI/GRE and coronal oblique T2 through the hippocampi. CT only in the emergency or when MRI is impossible. PET and ictal SPECT for surgical planning.

Antiseizure medication choice

Seizure type	First line	Avoid
Focal	Lamotrigine (SANAD II), levetiracetam; carbamazepine, oxcarbazepine, lacosamide, zonisamide	—
Generalised tonic-clonic	Valproate (SANAD II); levetiracetam or lamotrigine if valproate unsuitable	Carbamazepine, oxcarbazepine, phenytoin can worsen absence and myoclonus
Absence	Ethosuximide, valproate (lamotrigine is less effective — Glauser 2010)	Carbamazepine, oxcarbazepine, phenytoin, gabapentin, pregabalin, vigabatrin, tiagabine
Myoclonic	Valproate, levetiracetam; clonazepam, perampanel	Carbamazepine, oxcarbazepine, phenytoin, gabapentinoids; lamotrigine may worsen
Tonic/atonic (LGS)	Valproate, lamotrigine, rufinamide, clobazam, cannabidiol, fenfluramine	Carbamazepine, vigabatrin

Drug	Key adverse effects	Notes
Levetiracetam	Irritability, mood change, somnolence	Renal elimination; no significant interactions

Drug	Key adverse effects	Notes
Lamotrigine	Rash (SJS/TEN), dizziness, diplopia	Slow titration; halve with valproate; oestrogen lowers levels
Carbamazepine	Hyponatraemia, rash, leukopenia, hepatotoxicity	Autoinducer; HLA-B*15:02 screening in South-East Asian ancestry
Valproate	Weight gain, tremor, hair loss, hepatotoxicity, pancreatitis, hyperammonaemia	Highest teratogenic and neurodevelopmental risk; pregnancy prevention programme
Phenytoin	Gingival hyperplasia, hirsutism, ataxia, osteomalacia	Saturable (Michaelis–Menten) kinetics; narrow therapeutic index
Topiramate	Cognitive slowing, word-finding difficulty, weight loss, stones, angle-closure glaucoma	Carbonic anhydrase inhibitor
Lacosamide	Dizziness, diplopia, PR prolongation	IV form available
Zonisamide	Weight loss, stones, oligohidrosis	Sulfonamide

Special populations

Women. Pre-conception counselling at every visit. Folic acid before conception (0.4–5 mg depending on guideline; higher doses with valproate or enzyme inducers). Valproate must not be used in women of childbearing potential outside a pregnancy prevention programme; lamotrigine and levetiracetam have the most reassuring pregnancy data. Enzyme inducers reduce hormonal contraceptive efficacy; oestrogen halves lamotrigine levels. Catamenial epilepsy: seizures cluster around menstruation.

Older adults. Causes: stroke, neurodegeneration, tumour. Lamotrigine and levetiracetam are preferred; avoid phenytoin and phenobarbital (cognition, interactions, bone). Start low, go slow.

Status epilepticus

Convulsive status: 5 minutes or more of continuous seizure activity, or recurrent seizures without recovery between them (t1 = 5 min; t2 = 30 min, after which long-term consequences are likely).

Phase	Time	Intervention
Stabilisation	0–5 min	ABC, oxygen, monitoring, IV access, glucose; thiamine 100 mg IV if at risk
First line	5–20 min	Lorazepam 0.1 mg/kg IV (max 4 mg, may repeat once) or diazepam 0.15–0.2 mg/kg; midazolam 10 mg IM/IN/buccal if no IV access
Second line	20–40 min	Levetiracetam 60 mg/kg (max 4500 mg), fosphenytoin 20 mg PE/kg, or valproate 40 mg/kg — equivalent in ESETT (2019)
Refractory	40–60 min	Intubation, continuous EEG, anaesthetic infusion (midazolam, propofol, thiopental)
Super-refractory	> 24 h of anaesthesia	Ketamine, ketogenic diet, immunotherapy (consider NORSE/FIRES), pyridoxine in children

Surgery and neuromodulation

Refer when two appropriate, tolerated, adequately dosed drugs have failed (ILAE definition of drug resistance), or earlier when a resectable lesion is present.

Procedure	Indication	Outcome
Anterior temporal lobectomy	Mesial temporal sclerosis	60–70 % seizure-free; superior to medical therapy (Wiebe 2001: 58 % vs 8 % at 1 year)
Lesionectomy	Tumour, cavernoma, focal cortical dysplasia	Depends on completeness of resection

Procedure	Indication	Outcome
Laser interstitial thermal therapy	Mesial temporal targets, hypothalamic hamartoma	Less invasive; slightly lower freedom rates
Hemispherotomy	Hemimegalencephaly, Rasmussen encephalitis, large perinatal infarct	70–90 % seizure-free
Corpus callosotomy	Atonic drop attacks	Reduces drops and injuries
Vagus nerve stimulation	Drug-resistant, not resectable	~50 % responder rate after 1–2 years
Responsive neurostimulation	One or two unresectable foci, including bilateral mesial temporal	Median seizure reduction ~75 % at 9 years
Deep brain stimulation (anterior thalamic nucleus)	Drug-resistant focal epilepsy	Approved (EU 2010, FDA 2018); SANTE: 56 % median reduction at 2 years, improving over time

Functional (psychogenic non-epileptic) seizures

Paroxysmal events resembling epileptic seizures without epileptiform activity; a functional neurological disorder.

Feature	Epileptic	Functional
Onset	Abrupt	Often gradual
Duration	Usually < 2 min	Often > 2 min, fluctuating
Movements	Stereotyped, synchronous	Variable, asynchronous, side-to-side head movement, pelvic thrusting
Eyes	Usually open	Usually closed, resisting opening
Tongue biting	Lateral	Rare; tip
Afterwards	Confusion, drowsiness, stertorous breathing	Rapid recovery, often tearful

Diagnosis rests on a captured typical event on video-EEG. Treatment is explanation and psychotherapy; ASMs do not help.

Pattern recognition — Chapter 3

Sign	Description	Condition
Hippocampal sclerosis	Hippocampal atrophy, T2/FLAIR hyperintensity, loss of internal architecture	Mesial temporal lobe epilepsy
Transmantle sign	Funnel-shaped FLAIR signal from cortex to ventricle, cortical thickening, blurred grey–white junction	Focal cortical dysplasia type IIb
Interictal PET hypometabolism	Focal temporal hypometabolism	Epileptogenic temporal focus

Movement Disorders

Key tables: Parkinson's disease features · MDS 2015 criteria · Hoehn and Yahr · Atypical parkinsonism · Dystonia classification · Huntington's genetics

Movement disorders affect the speed, quality and ease of movement. They divide into hypokinetic (parkinsonism) and hyperkinetic (tremor, chorea, dystonia, myoclonus, tics) disorders.

Pathophysiology	Basal ganglia circuit dysfunction
Key structures	Striatum (caudate, putamen), globus pallidus, substantia nigra, subthalamic nucleus
Approach	Name the movement, find the associated features, then the cause

Parkinson's disease

A progressive neurodegenerative disorder with loss of dopaminergic neurons in the substantia nigra pars compacta and α -synuclein (Lewy) pathology. The second commonest neurodegenerative disease after Alzheimer's.

Feature	Description
Bradykinesia	Slowness with progressive decrement of speed and amplitude on repetition — essential for diagnosis
Rest tremor	4–6 Hz, pill-rolling, usually starting in one hand; suppressed by movement, re-emerges with posture
Rigidity	Velocity-independent; cogwheeling when tremor is superimposed
Postural instability	A late feature; early falls point to atypical parkinsonism (not an MDS core feature)

Associated features. Motor: micrographia, hypophonia, hypomimia, dysphagia, shuffling gait, reduced arm swing, freezing. Non-motor: REM sleep behaviour disorder, hyposmia, constipation and depression can precede motor signs by years; also anxiety, apathy, cognitive decline, daytime sleepiness, orthostatic hypotension, urinary urgency, seborrhoea.

MDS clinical diagnostic criteria (Postuma 2015)

The current standard; the UK Brain Bank criteria remain in older texts.

1. **Parkinsonism:** bradykinesia plus rest tremor and/or rigidity.
2. **Absolute exclusion criteria** absent — e.g. unequivocal cerebellar signs, downward vertical supranuclear gaze palsy, probable bvFTD or PPA within 5 years, parkinsonism restricted to the legs for > 3 years, treatment with a dopamine blocker, no response to high-dose levodopa, cortical sensory loss or limb apraxia, normal presynaptic dopaminergic imaging.
3. **Supportive criteria:** clear and dramatic levodopa response; levodopa-induced dyskinesia; rest tremor of a limb; olfactory loss **or** cardiac sympathetic denervation on MIBG scintigraphy.
4. **Red flags** — e.g. rapid progression to wheelchair, early severe bulbar dysfunction or autonomic failure, recurrent falls within 3 years, inspiratory stridor, no progression over 5 years, symmetric onset.

Clinically established PD: no exclusions, ≥ 2 supportive criteria, no red flags. **Clinically probable PD:** no exclusions; red flags (at most two) are counterbalanced by an equal number of supportive criteria.

Hoehn and Yahr	Description
1	Unilateral involvement
1.5	Unilateral plus axial involvement
2	Bilateral without balance impairment
2.5	Mild bilateral disease, recovers on pull test

Hoehn and Yahr	Description
3	Mild-moderate bilateral disease, some postural instability, physically independent
4	Severe disability; can still walk or stand unassisted
5	Wheelchair-bound or bedridden unless aided

Treatment

Drug	Typical dosing	Notes
Levodopa/carbidopa (or benserazide)	Start 100/25 mg three times daily	Most effective; no evidence that early use accelerates progression (LEAP 2022)
Dopamine agonists (pramipexole, ropinirole, rotigotine patch)	Titrated	Fewer early dyskinesias; impulse control disorders, sleep attacks, oedema, hallucinations
MAO-B inhibitors (rasagiline, selegiline, safinamide)	Rasagiline 1 mg daily	Modest symptomatic benefit; disease modification not proven (ADAGIO 2009 inconclusive)
COMT inhibitors (entacapone, opicapone)	With each levodopa dose / once daily	Adjunct for wearing-off
Amantadine	100 mg two to three times daily	Treats levodopa-induced dyskinesia
Anticholinergics (trihexyphenidyl)	1–2 mg, titrated	Young, tremor-predominant; avoid in the elderly

Motor complication	Description	Management
Wearing-off	Benefit fades before the next dose	More frequent levodopa; add COMT or MAO-B inhibitor or agonist
On-off fluctuations	Unpredictable switching	Agonist, apomorphine, device-aided therapy (levodopa-carbidopa intestinal gel, subcutaneous foslevodopa/foscarbidopa, apomorphine infusion), DBS
Dyskinesia	Peak-dose (commonest), diphasic, off-period dystonia	Smaller, more frequent doses; amantadine; DBS
Freezing of gait	Sudden inability to step, worse at turns and doorways	Visual and auditory cues; optimise levodopa

Deep brain stimulation (STN or GPi). Candidates: clear levodopa response, disabling fluctuations or dyskinesia, or drug-resistant tremor; no significant dementia or uncontrolled psychiatric disease. Reduces off-time and dyskinesia (STN also lowers medication). Haemorrhage 1–2 %, infection, hardware problems, speech and mood effects. Levodopa-unresponsive symptoms (except tremor) do not improve.

Atypical parkinsonism

	MSA	PSP	CBS
Pathology	α -synuclein (glial cytoplasmic inclusions)	4-repeat tau	Variable — CBD (4R tau), PSP, Alzheimer's, others
Hallmark	Early severe autonomic failure; MSA-P or MSA-C	Vertical supranuclear gaze palsy (downgaze, slowed vertical saccades first); falls within the first year	Strikingly asymmetric limb apraxia, alien limb, cortical sensory loss, myoclonus, dystonia
Other clues	Stridor, RBD, antecollis, cold hands, pyramidal signs	Axial > limb rigidity, retrocollis, "surprised" stare with procerus sign, applause sign, frontal dysexecutive syndrome, pseudobulbar affect	Asymmetric frontoparietal atrophy
Levodopa	Poor or transient (up to a third respond early)	Poor	Poor

	MSA	PSP	CBS
Imaging	Hot cross bun (MSA-C), putaminal rim and atrophy (MSA-P), middle cerebellar peduncle atrophy	Hummingbird and morning-glory (Mickey Mouse) signs; midbrain/pons ratio reduced	Asymmetric atrophy

Corticobasal syndrome vs degeneration. *Corticobasal syndrome* is the clinical picture; *corticobasal degeneration* is one of its pathologies. Only about half of CBS cases have CBD at autopsy.

Dementia with Lewy bodies — see Chapter 10.

Essential tremor

The commonest movement disorder: bilateral, largely symmetric action (postural and kinetic) tremor of the hands and forearms.

MDS 2018 definition. Isolated bilateral upper-limb action tremor for ≥ 3 years, with or without tremor elsewhere (head, voice, legs), and no other neurological signs. "ET plus" when soft signs coexist (impaired tandem gait, questionable dystonic posturing, mild memory impairment, rest tremor).

Feature	Essential tremor	Parkinson's disease
Tremor	Action (postural, kinetic)	Rest
Onset	Bilateral	Unilateral
Frequency	4–12 Hz	4–6 Hz
Other signs	None	Bradykinesia, rigidity
Alcohol	Often improves	No effect
Family history	Common (~50 %)	Less common
DaT-SPECT	Normal	Abnormal

Treatment	Dosing	Notes
Propranolol	40 mg twice daily, up to 120–240 mg/day	First line; avoid in asthma, bradycardia
Primidone	25 mg at night, up to 250 mg twice daily	First line; start very low (acute sedation, nausea)
Topiramate	Up to 100 mg twice daily	Second line; cognitive effects
Gabapentin	1200–1800 mg/day	Second line

Refractory: VIM thalamic DBS or MR-guided focused ultrasound thalamotomy.

Dystonia

Sustained or intermittent muscle contractions causing abnormal, often repetitive movements, postures or both; often patterned, twisting, triggered by voluntary action, and improved by sensory tricks (geste antagoniste).

Classification (consensus 2013)

Axis I — clinical features.

- Age at onset: infancy (0–2 y), childhood (3–12), adolescence (13–20), early adulthood (21–40), late adulthood (> 40).
- Distribution: focal, segmental (contiguous), multifocal (non-contiguous), generalised (trunk + ≥ 2 other sites), hemidystonia.
- Temporal pattern: static or progressive; persistent, action-specific, diurnal or paroxysmal.
- Associated features: isolated or combined (with parkinsonism, myoclonus, etc.).

Axis II – aetiology. Nervous-system pathology (degenerative, static lesion, none); inherited, acquired or idiopathic.

Early-onset generalised dystonia: test for *TOR1A* (DYT1), and always give a levodopa trial (dopa-responsive dystonia, *GCH1*).

Focal dystonia	Description	Treatment
Cervical dystonia	Commonest focal dystonia; torticollis, laterocollis, antero-/retrocollis, dystonic head tremor	Botulinum toxin
Blepharospasm	Forced eye closure; functional blindness	Botulinum toxin
Oromandibular	Jaw opening or closing, tongue protrusion	Botulinum toxin
Laryngeal (spasmodic dysphonia)	Adductor (strained voice) or abductor (breathy)	Botulinum toxin
Writer's cramp	Task-specific hand dystonia	Botulinum toxin, adaptive devices
Musician's dystonia	Task-specific	Retraining, botulinum toxin

Treatment. Botulinum toxin first line for focal dystonia; trihexyphenidyl (best in young patients), baclofen, clonazepam; GPI-DBS for refractory generalised or segmental dystonia (best results in *TOR1A*).

Huntington's disease

Autosomal dominant; CAG repeat expansion in *HTT* (chromosome 4p). Chorea, cognitive decline and psychiatric disease; caudate atrophy.

Domain	Features
Motor	Chorea early; dystonia, parkinsonism and bradykinesia later; motor impersistence (milkmaid grip); slow saccades
Cognitive	Executive dysfunction, poor planning, slowed processing; dementia late
Psychiatric	Depression, apathy, irritability, psychosis, suicide risk
Other	Weight loss, sleep disturbance

CAG repeats	Meaning
≤ 26	Normal
27–35	Intermediate — not affected, but may expand in offspring
36–39	Reduced penetrance
≥ 40	Full penetrance
> 60	Juvenile onset (Westphal variant: rigidity, seizures); usually paternal transmission (anticipation)

Treatment. Chorea: VMAT2 inhibitors (tetrabenazine, deutetrabenazine, valbenazine — watch depression and suicidality) or antipsychotics. Psychiatric: SSRIs, antipsychotics. Multidisciplinary care and genetic counselling.

Tics and Tourette syndrome

Tics are sudden, rapid, recurrent, non-rhythmic movements or vocalisations, preceded by a premonitory urge, temporarily suppressible, waxing and waning. **Tourette syndrome:** multiple motor tics and at least one vocal tic, onset before 18, present for > 1 year.

- Coprolalia in < 10–20 %.
- Comorbidity: ADHD (~50–60 %), OCD (30–50 %), anxiety, learning difficulties.
- Treatment: education first; behavioural therapy (CBIT) first line; α2 agonists (clonidine, guanfacine), aripiprazole or risperidone, topiramate; botulinum toxin for focal tics; DBS in severe refractory adults.

Pattern recognition — Chapter 4

Sign	Description	Condition
Hot cross bun	Cruciform T2 hyperintensity in the pons	MSA (especially MSA-C); not specific (also SCAs)
Putaminal rim	T2 hyperintense lateral putaminal rim with putaminal hypointensity	MSA-P
Hummingbird (penguin)	Midbrain tegmental atrophy with preserved pons on midsagittal MRI	PSP
Morning glory / Mickey Mouse	Concave lateral midbrain tegmentum on axial MRI	PSP
Swallow-tail sign loss	Loss of nigrosome-1 hyperintensity on high-resolution SWI	Parkinson's disease
Face of the giant panda	T2 midbrain signal with sparing of red nuclei and lateral pars reticulata	Wilson's disease
Eye-of-the-tiger	Pallidal T2 hypointensity with central hyperintensity	PKAN (<i>PANK2</i>)
Box-car ventricles	Caudate atrophy widening the frontal horns	Huntington's disease

Multiple Sclerosis and Demyelinating Diseases

Key tables: McDonald 2017 (and 2024 revision) · Clinical courses · MRI features · Disease-modifying therapies · NMOSD vs MOGAD vs MS

Multiple sclerosis is the commonest demyelinating disease of the central nervous system.

Definition	Immune-mediated inflammatory demyelination and neurodegeneration of the CNS
Prevalence	~2.8 million worldwide; higher at higher latitudes
Onset	Peak 20–40 years; F:M about 3:1
Pathology	Demyelinating plaques, inflammation, axonal loss, gliosis
Risk factors	Low vitamin D, smoking, obesity in adolescence, EBV infection (necessary for nearly all MS), HLA-DRB1*15:01

Clinical features

Presentation	Description	Frequency at onset
Optic neuritis	Subacute unilateral visual loss, pain on eye movement, colour desaturation, RAPD	~20 %
Sensory	Numbness, paraesthesia, Lhermitte's sign	~30–40 %
Motor	Monoparesis, paraparesis	~15 %
Brainstem/cerebellar	Diplopia, internuclear ophthalmoplegia, vertigo, ataxia	~15 %
Bladder and bowel	Urgency, frequency, retention	Common over the course
Fatigue	Disproportionate to activity	~80 % over the course

Uhthoff's phenomenon. Transient worsening with a rise in body temperature (exercise, heat, fever), from temperature-sensitive conduction block in demyelinated axons.

Clinical courses (Lublin 2013)

Phenotype	Description
Clinically isolated syndrome (CIS)	First episode suggestive of demyelination, not yet fulfilling MS criteria
Relapsing–remitting (RRMS)	~85 % at onset; attacks with full or partial recovery
Secondary progressive (SPMS)	Progression after an initial relapsing course
Primary progressive (PPMS)	~10–15 %; progression from onset

Each course is further described as **active** (relapses or new MRI activity) or not, and **progressing** or not. *Progressive–relapsing MS has been retired* – it is now PPMS with activity. Radiologically isolated syndrome (RIS) describes typical lesions found incidentally without symptoms.

Diagnosis — McDonald 2017

The clinical picture must be typical and there must be no better explanation. MS requires **dissemination in space (DIS)** and **dissemination in time (DIT)**.

DIS: ≥ 1 T2 lesion in ≥ 2 of 4 regions — periventricular, **cortical or juxtacortical**, infratentorial, spinal cord. Symptomatic and asymptomatic lesions both count.

DIT: simultaneous enhancing and non-enhancing lesions on any scan; or a new T2 or enhancing lesion on follow-up; or a second attack. **CSF-specific oligoclonal bands can substitute for DIT** in a patient with a typical CIS who meets DIS.

Clinical presentation	Additional data needed
≥ 2 attacks, objective evidence of ≥ 2 lesions	None
≥ 2 attacks, objective evidence of 1 lesion	DIS: a further attack in a different site, or MRI
1 attack, objective evidence of ≥ 2 lesions	DIT: a further attack, MRI, or CSF-specific OCBs
1 attack, objective evidence of 1 lesion	DIS and DIT (DIT by MRI or OCBs)
PPMS	1 year of progression plus 2 of: ≥ 1 brain lesion in a typical region; ≥ 2 spinal cord lesions; CSF-specific OCBs

2024 revision of the McDonald criteria (ECTRIMS 2024, published 2025). Optic nerve added as a fifth DIS region; central vein sign and paramagnetic rim lesions accepted as MS-specific supportive markers; kappa free light chain index accepted as an alternative to OCBs; DIT no longer required in selected settings; criteria applicable to RIS, older people and children. Check which edition the examination uses — most question banks still test McDonald 2017.

MRI features

Feature	Description
Ovoid periventricular lesions	Perpendicular to the ventricles — Dawson's fingers
Juxtacortical and cortical	Involve U-fibres or cortex
Infratentorial	Pons (surface), middle cerebellar peduncle, cerebellum
Calloseseptal	Undersurface of the corpus callosum
Spinal cord	Usually < 2 vertebral segments, peripheral, $< 1/2$ the cord's cross-section; commonest cervical
Enhancement	Active inflammation; open ring (incomplete, open towards cortex) typical of demyelination
T1 black holes	Persistent T1 hypointensity — axonal loss
Central vein sign	Vein in the lesion centre on SWI/FLAIR*; visible at 3 T
Paramagnetic rim lesions	Iron rim on SWI — chronic active, smouldering lesions

Differential diagnosis

Condition	Clues
NMOSD	Longitudinally extensive transverse myelitis (≥ 3 segments), severe optic neuritis, area postrema syndrome, AQP4-IgG
MOGAD	Bilateral or anterior optic neuritis with disc swelling, ADEM, conus myelitis, MOG-IgG
ADEM	Monophasic, post-infectious, children, encephalopathy

Condition	Clues
Sarcoidosis	Leptomeningeal and pachymeningeal enhancement, hilar nodes
Behçet's	Oral/genital ulcers, uveitis; brainstem lesions
Primary CNS vasculitis	Infarcts in several territories, headache, cognitive decline; biopsy
Small-vessel disease, migraine	Punctate subcortical lesions, no enhancement, no CVS
B12 or copper deficiency	Dorsal column myelopathy
Susac syndrome	Encephalopathy, branch retinal artery occlusion, hearing loss; central callosal "snowball" lesions

Treatment

Relapse. Methylprednisolone 500–1000 mg IV (or high-dose oral) daily for 3–5 days; plasma exchange for severe steroid-refractory relapses. Steroids hasten recovery but do not change long-term disability.

Disease-modifying therapies

Category	Drugs	Key risks
Injectable (moderate efficacy)	Interferon-β, glatiramer acetate	Flu-like symptoms, LFTs, depression (IFN); injection-site reactions (GA)
Oral (moderate)	Teriflunomide	Hepatotoxicity, teratogenicity (accelerated elimination)
Oral (moderate)	Dimethyl and diroximel fumarate	Flushing, GI upset, lymphopenia, PML
Oral (moderate–high)	S1P modulators — fingolimod, siponimod (active SPMS), ozanimod, ponesimod	First-dose bradycardia, macular oedema, infections, rebound on stopping
Oral (high, pulsed)	Cladribine	Lymphopenia, herpes zoster, teratogenicity
Infusion (high)	Natalizumab	PML (JCV antibody index, > 2 years, prior immunosuppression)
Anti-CD20 (high)	Ocrelizumab (only licensed DMT for PPMS — ORATORIO), ofatumumab (SC), ublituximab; rituximab off-label	Infusion reactions, infections, hypogammaglobulinaemia
Infusion (high)	Alemtuzumab	Thyroid disease, ITP, anti-GBM disease, stroke
Rescue	Autologous haematopoietic stem-cell transplantation	Treatment-related mortality; highly active RRMS

Mitoxantrone is now obsolete (cardiotoxicity, leukaemia).

Symptom	Treatment
Fatigue	Exercise, energy management; amantadine or modafinil (weak evidence)
Spasticity	Baclofen, tizanidine, gabapentin, nabiximols, botulinum toxin; intrathecal baclofen
Bladder	Antimuscarinics, mirabegron, intermittent self-catheterisation, intravesical botulinum toxin
Walking	Fampridine (dalfampridine)
Pain	Gabapentinoids, TCAs, SNRIs; carbamazepine for trigeminal neuralgia
Depression	SSRIs, SNRIs, psychotherapy

Related disorders

	NMOSD (AQP4)	MOGAD	MS
Target	Aquaporin-4 on astrocytes	MOG on oligodendrocytes	—
Optic neuritis	Severe, posterior, chiasmal, bilateral; poor recovery	Bilateral, anterior with disc swelling; good recovery	Unilateral, mild, short segment

	NMOSD (AQP4)	MOGAD	MS
Myelitis	LETM ≥ 3 segments, central	LETM or short, conus involvement	Short, peripheral
Brain	Area postrema, periependymal, diencephalic	ADEM-like, fluffy, cortical encephalitis	Ovoid periventricular, juxtacortical
CSF OCBs	Usually absent	Usually absent	Present in > 90 %
Maintenance	Eculizumab, ravulizumab, inebilizumab, satralizumab; rituximab	Often monophasic; IVIG, rituximab, steroids for relapsing disease	MS DMTs

NMOSD core clinical characteristics (Wingerchuk 2015): optic neuritis, acute myelitis, area postrema syndrome (intractable hiccups or vomiting), acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic syndrome with typical lesions, symptomatic cerebral syndrome with typical lesions. With AQP4-IgG, one core characteristic is enough. Some MS DMTs (interferon, natalizumab, fingolimod) **worsen** NMOSD.

ADEM. Monophasic, often post-infectious, children more than adults. Encephalopathy is required; multifocal deficits, seizures. Large, poorly demarcated, bilateral white- and deep grey-matter lesions of similar age. High-dose steroids; IVIG or PLEX if refractory. Test for MOG-IgG.

Pattern recognition — Chapter 5

Sign	Description	Condition
Dawson's fingers	Ovoid lesions perpendicular to the lateral ventricles	MS
Open ring	Incomplete ring enhancement, open towards cortex	Demyelination (MS, tumefactive MS)
T1 black holes	Persistent T1 hypointense lesions	Axonal loss in chronic MS
Central vein sign	Central vessel within lesions on SWI	MS (vs mimics)
Paramagnetic rim lesion	Hypointense iron rim on SWI	Chronic active MS lesion
Longitudinally extensive myelitis	Cord lesion ≥ 3 vertebral segments	NMOSD (also MOGAD), not MS
Bright spotty lesions	Very T2-hyperintense spots in the cord	NMOSD
H-sign	Grey-matter-restricted cord signal on axial images	MOGAD

Neuromuscular Disorders

Key tables: Localisation in the motor unit · ALS criteria · GBS and CIDP · Myasthenia antibodies and treatment · Inflammatory myopathies

Neuromuscular disorders affect the motor unit: anterior horn cell, root, plexus, peripheral nerve, neuromuscular junction and muscle.

Localisation

Site	Weakness	Atrophy	Fasciculations	Sensory	Reflexes
Muscle	Proximal > distal	Mild, late	None	Normal	Normal, reduced late
Neuromuscular junction	Fatigable, fluctuating; ocular and bulbar	None	None	Normal	Normal (reduced in LEMS, with post-exercise facilitation)
Peripheral nerve	Distal > proximal	Moderate	Occasional	Abnormal	Reduced or absent
Root	Myotomal	Variable	Occasional	Dermatomal	Reduced at that level
Plexus	Several nerves and roots	Variable	Occasional	Several nerves	Variable
Anterior horn cell	Proximal and distal, asymmetric	Marked	Prominent	Normal	Reduced (brisk if UMN also involved)

Amyotrophic lateral sclerosis

Progressive degeneration of upper and lower motor neurons; the commonest adult motor neuron disease.

- UMN and LMN signs in the same region: weakness, wasting, fasciculations, with spasticity and brisk reflexes.
- Limb onset ~70 %, bulbar onset ~25 % (dysarthria, dysphagia, tongue wasting and fasciculation, emotional lability).
- Spared: eye movements, sphincters, sensation (largely).
- Frontotemporal dementia in 10–15 %; cognitive or behavioural impairment in up to half.
- Genetics: ~10 % familial. *C9orf72* repeat expansion (commonest, ALS-FTD), *SOD1*, *TARDBP*, *FUS*.

Diagnostic criteria. The **Gold Coast criteria (2020)** are now preferred: progressive motor impairment, plus UMN and LMN dysfunction in at least one region **or** LMN dysfunction in at least two regions, plus exclusion of other disease. They replace the graded categories of revised El Escorial/Awaji, which remain in older texts (definite = UMN + LMN in 3 regions).

Mimic	Distinguishing features
Cervical spondylotic myelopathy	Neck pain, radicular sensory signs, no bulbar or tongue involvement; MRI
Multifocal motor neuropathy	Pure LMN, upper limb, along named nerves; conduction block; anti-GM1 IgM; IVIG-responsive
Kennedy disease (SBMA)	X-linked, AR CAG expansion; bulbar and facial weakness, perioral fasciculation, gynaecomastia, sensory neuropathy
Inclusion body myositis	Finger flexor and quadriceps weakness, raised CK, myopathic EMG
Hexosaminidase A deficiency (adult GM2)	Young onset, psychiatric features, cerebellar atrophy
Post-polio syndrome	History of polio, decades of stability

Treatment	Notes
Riluzole 50 mg twice daily	Glutamate modulation; prolongs survival by ~2–3 months
Edaravone	Free radical scavenger (IV or oral); approved in the US, not in the EU
Tofersen	Intrathecal antisense oligonucleotide for <i>SOD1</i> -ALS (FDA 2023, EMA 2024)
Non-invasive ventilation	When FVC < 50 %, orthopnoea, SNIP or nocturnal hypoventilation; prolongs survival
Gastrostomy	Before FVC falls below 50 % and with > 10 % weight loss
Multidisciplinary clinic	Improves survival and quality of life; advance care planning

Peripheral neuropathy

Axis	Categories
Fibre type	Large fibre (vibration, proprioception, motor), small fibre (pain, temperature, autonomic), mixed
Pathology	Axonal vs demyelinating
Distribution	Length-dependent; non-length-dependent (polyradiculoneuropathy, ganglionopathy); mononeuropathy, mononeuritis multiplex
Tempo	Acute (< 4 weeks), subacute (4–8 weeks), chronic (> 8 weeks)

Category	Causes
Metabolic	Diabetes (commonest), uraemia, hypothyroidism
Toxic	Alcohol, chemotherapy (vincristine, cisplatin, taxanes, bortezomib), metronidazole, nitrous oxide
Nutritional	B12, copper, thiamine, B6 deficiency (and B6 excess)
Immune	GBS, CIDP, vasculitis, Sjögren's (sensory ganglionopathy)
Hereditary	CMT, HNPP, hereditary transthyretin amyloidosis
Infectious	HIV, leprosy, hepatitis C, Lyme
Paraprotein	MGUS (anti-MAG), myeloma, POEMS, AL amyloid

Guillain–Barré syndrome

Acute immune polyradiculoneuropathy, usually 1–4 weeks after infection (*Campylobacter jejuni*, CMV, EBV, Zika). Nadir within 4 weeks.

- Ascending symmetric weakness, areflexia, sensory symptoms, back or radicular pain; facial and bulbar weakness; dysautonomia.
- Variants: AIDP, AMAN and AMSAN (axonal; anti-GM1/GD1a), Miller Fisher (ophthalmoplegia, ataxia, areflexia; anti-GQ1b), pharyngeal–cervical–brachial, Bickerstaff brainstem encephalitis.
- CSF: albuminocytological dissociation – may be normal in the first week; > 50 cells/μL argues against GBS.
- NCS: demyelinating or axonal pattern; sural sparing.

Respiratory monitoring. FVC, maximal inspiratory and expiratory pressure. **20/30/40 rule:** consider intubation if FVC < 20 mL/kg, MIP weaker than –30 cmH₂O, or MEP < 40 cmH₂O, or with bulbar failure. EGRIS predicts ventilation; mEGOS predicts outcome.

Treatment. IVIG 2 g/kg over 5 days or plasma exchange (5 exchanges) – equally effective, not additive; best within 2 weeks of onset in patients unable to walk 10 m unaided. A second IVIG course is not recommended (SID-GBS). Corticosteroids do not help. Watch for autonomic instability, pain and thromboembolism. Treatment-related fluctuation within 8 weeks is common; three or more, or deterioration after 8 weeks, suggests acute-onset CIDP.

Chronic inflammatory demyelinating polyradiculoneuropathy

Progression or relapses over ≥ 8 weeks; symmetric proximal and distal weakness, sensory loss and areflexia.

EAN/PNS guideline 2021. Two diagnostic levels only: **CIDP** and **possible CIDP** (the old "definite/probable" tiers are gone). *Typical CIDP* and *CIDP variants* — distal (DADS), multifocal (Lewis–Sumner), focal, motor, sensory. Diagnosis needs motor conduction criteria in ≥ 2 nerves (or ≥ 1 nerve plus supportive criteria for possible CIDP), with sensory conduction abnormalities in ≥ 2 nerves. Supportive: raised CSF protein with < 10 cells, MRI or ultrasound nerve root/plexus enlargement, objective response to treatment, nerve biopsy. Test for nodal/paranodal antibodies (NF155, CNTN1, Caspr1, NF186) — **autoimmune nodopathies** are now separate from CIDP and respond to rituximab rather than IVIG.

Treatment. IVIG, corticosteroids or plasma exchange as first line; subcutaneous immunoglobulin for maintenance; efgartigimod (ADHERE 2024). Exclude POEMS (VEGF, λ paraprotein) and anti-MAG neuropathy.

Myasthenia gravis

Autoimmune disorder of the postsynaptic neuromuscular junction.

- Fatigable, fluctuating weakness; worse later in the day.
- Ocular onset in $\sim 85\%$ (ptosis, diplopia); $\sim 50\%$ of purely ocular disease generalises, usually within 2 years.
- Bulbar, neck-flexor and proximal limb weakness; respiratory failure (crisis).
- Reflexes and sensation normal; pupils spared.

Antibody	Frequency	Features
AChR	$\sim 85\%$ of generalised, $\sim 50\%$ of ocular MG	Thymic hyperplasia (early onset) or thymoma ($\sim 10\text{--}15\%$)
MuSK	$\sim 5\text{--}8\%$	Women; bulbar, neck and respiratory weakness, facial and tongue atrophy; poor response to and intolerance of pyridostigmine; excellent response to rituximab; no thymectomy benefit
LRP4	1–3 %	Milder, often ocular
Seronegative	$\sim 5\text{--}10\%$	Test with cell-based assays
Titin, ryanodine receptor	—	Markers of thymoma and late-onset disease

Diagnosis. Antibodies; repetitive nerve stimulation at 3 Hz ($> 10\%$ decrement); single-fibre EMG (increased jitter — most sensitive); ice-pack test for ptosis (≥ 2 mm improvement). The edrophonium (Tensilon) test is obsolete. CT or MRI of the chest for thymoma.

Category	Treatment	Notes
Symptomatic	Pyridostigmine	First line; cholinergic side effects
Immunotherapy	Prednisolone	Start low and increase in outpatients — high initial doses cause transient worsening
Steroid-sparing	Azathioprine, mycophenolate, methotrexate, tacrolimus	Slow onset (months)
Acute (crisis, pre-operative)	IVIG or plasma exchange	PLEX works slightly faster
Thymectomy	Thymoma — always. Non-thymomatous AChR+ generalised MG, age 18–65	MGTX (2016): better clinical scores and lower steroid needs at 3 years
Complement inhibitors	Eculizumab, ravulizumab, zilucoplan	AChR+ generalised MG; meningococcal vaccination
FcRn antagonists	Efgartigimod, rozanolixizumab, nipocalimab	Lower IgG; AChR+ (rozanolixizumab and nipocalimab also MuSK+)
B-cell depletion	Rituximab	MuSK+ MG especially

Drugs that worsen MG: aminoglycosides, fluoroquinolones, macrolides, magnesium, β -blockers, neuromuscular blockers, immune checkpoint inhibitors (which can also trigger MG with myositis and myocarditis).

Feature	Myasthenic crisis	Cholinergic crisis (rare)
Cause	Infection, surgery, drug change, steroid start	Excess cholinesterase inhibitor
Pupils	Normal	Miotic
Secretions	Normal	Increased — salivation, lacrimation, bronchorrhoea
GI	None	Cramps, diarrhoea, vomiting
Muscle	Weakness	Weakness with fasciculations
Treatment	Secure airway, IVIG or PLEX, treat trigger	Stop cholinesterase inhibitor, supportive care, atropine

In practice, any weak, deteriorating myasthenic patient is managed as a crisis; pyridostigmine is usually withheld while ventilated.

Lambert–Eaton myasthenic syndrome. Antibodies to P/Q-type voltage-gated calcium channels; ~50–60 % paraneoplastic (small-cell lung cancer). Proximal leg weakness, areflexia with post-exercise facilitation, autonomic symptoms (dry mouth). Low CMAP with > 100 % increment after 10 s of exercise or 50 Hz stimulation. Amifampridine (3,4-DAP); treat the tumour.

Myopathy

Proximal symmetric weakness, normal sensation, reflexes kept until late, no fasciculations.

Category	Examples
Muscular dystrophies	Duchenne, Becker, facioscapulohumeral (FSHD), myotonic dystrophy types 1 and 2, limb-girdle
Inflammatory	Dermatomyositis, immune-mediated necrotising myopathy, antisynthetase syndrome, inclusion body myositis, overlap myositis
Metabolic	Pompe (acid maltase), McArdle (myophosphorylase), CPT2 deficiency, mitochondrial
Endocrine	Hypo- and hyperthyroidism, Cushing's and steroid myopathy, hyperparathyroidism
Toxic	Statins, colchicine, alcohol, zidovudine, immune checkpoint inhibitors
Congenital	Central core (<i>RYR1</i> , malignant hyperthermia), nemaline, centronuclear
Channelopathies	Hypo- and hyperkalaemic periodic paralysis, myotonia congenita

Inflammatory myopathy	Features	Antibodies
Dermatomyositis	Heliotrope rash, Gottron's papules, nailfold changes; perifascicular atrophy	Mi-2 (classic, good prognosis), MDA5 (amyopathic, rapidly progressive ILD), TIF1- γ and NXP2 (cancer association in adults), SAE
Antisynthetase syndrome	Myositis, ILD, arthritis, mechanic's hands, Raynaud's, fever	Jo-1 and other antisynthetases
Immune-mediated necrotising myopathy	Severe weakness, very high CK, necrosis with little inflammation	HMGCR (statin-associated), SRP
Inclusion body myositis	Over 50; asymmetric finger flexor and quadriceps weakness, dysphagia; rimmed vacuoles	cN1A (NT5C1A) — not specific
Polymyositis	A diagnosis of exclusion; most cases are reclassified	—

Investigation. CK (normal in some metabolic and steroid myopathies); EMG (short, small, polyphasic MUAPs; fibrillations in inflammatory disease); muscle MRI for pattern and biopsy site; biopsy; antibodies; genetics. Screen dermatomyositis for cancer.

Treatment. Corticosteroids plus a steroid-sparing agent (methotrexate, azathioprine, mycophenolate); IVIG (ProDERM for dermatomyositis); rituximab. IBM does not respond to immunotherapy.

Pattern recognition — Chapter 6

Sign	Description	Condition
Medial scapular winging	Inferior angle moves medially on pushing forwards	Serratus anterior — long thoracic nerve
Lateral scapular winging	On abduction	Trapezius — spinal accessory nerve
Scapular winging with facial weakness	Bilateral asymmetric winging, inability to whistle	FSHD
Popeye sign	Bunched biceps belly in the distal arm	Proximal (long-head) biceps tendon rupture; "Popeye arms" with forearm sparing in FSHD
Inverted champagne bottle	Distal leg wasting with preserved thighs	Charcot-Marie-Tooth disease
Gowers' sign	Climbing up the legs to stand	Proximal weakness — Duchenne
Calf pseudohypertrophy	Enlarged, firm calves	Duchenne and Becker
Split-hand sign	Thenar and first dorsal interosseous wasting with hypothenar sparing	ALS
Beevor's sign	Umbilicus moves up on neck flexion	Lower abdominal weakness — FSHD, T10 lesion

Headache and Facial Pain

Key tables: Red flags · ICHD-3 migraine criteria · Acute and preventive treatment · Trigeminal autonomic cephalalgias · IIH and GCA

Classification	Primary (migraine, tension-type, TACs) vs secondary (underlying cause) — ICHD-3 (2018)
Burden	Migraine is the second leading cause of years lived with disability worldwide
Approach	History first; image when red flags are present

Red flags — SNNOOP10 (simplified)

Flag	Concern
Systemic symptoms, fever, cancer, immunosuppression	Meningitis, metastasis, GCA
Neurological deficit or reduced consciousness	Mass, stroke, encephalitis
Onset sudden — thunderclap, peak within 1 minute	SAH, RCVS, dissection, CVST, pituitary apoplexy
Older age — new headache over 50	GCA, mass, subdural
Pattern change or progressive headache	Mass, IIH
Positional	Low-pressure (worse upright) or high-pressure (worse lying)
Precipitated by Valsalva, cough or exertion	Chiari I, posterior fossa lesion, SAH
Papilloedema	Raised ICP
Pregnancy or puerperium	CVST, pre-eclampsia, RCVS, apoplexy
Painful eye with autonomic features	Acute angle-closure glaucoma
Post-traumatic, Pathology of the immune system, Painkiller overuse	Subdural, opportunistic infection, MOH

Migraine

Recurrent attacks of 4–72 h; about 15 % of the population; F:M 3:1.

ICHD-3 migraine without aura. ≥ 5 attacks; 4–72 h untreated; ≥ 2 of unilateral, pulsating, moderate–severe, aggravated by routine activity; ≥ 1 of nausea/vomiting or photophobia **and** phonophobia.

Migraine with aura. ≥ 2 attacks of fully reversible visual, sensory, speech, motor, brainstem or retinal symptoms, with ≥ 3 of: spreads gradually over ≥ 5 min; ≥ 2 symptoms in succession; each lasts 5–60 min; ≥ 1 unilateral; ≥ 1 positive; headache within 60 min.

Aura	Description
Visual (> 90 %)	Fortification spectra, scintillating scotoma
Sensory	Cheiro-oral paraesthesia spreading over minutes
Speech	Dysphasia
Motor	Hemiplegic migraine — familial (<i>CACNA1A</i> , <i>ATP1A2</i> , <i>SCN1A</i>) or sporadic
Brainstem	≥ 2 of dysarthria, vertigo, tinnitus, hypacusis, diplopia, ataxia, reduced consciousness — no motor or retinal symptoms
Retinal	Monocular

Chronic migraine. Headache on ≥ 15 days/month for > 3 months, with migraine features on ≥ 8 days.

Acute treatment	Examples	Notes
NSAIDs, aspirin, paracetamol	Ibuprofen 400 mg, aspirin 900–1000 mg	Mild–moderate attacks
Triptans	Sumatriptan, rizatriptan, zolmitriptan, eletriptan	Early in the headache phase; contraindicated in coronary, cerebrovascular and peripheral vascular disease, uncontrolled hypertension
Antiemetics	Metoclopramide, domperidone, prochlorperazine	Nausea and gastric stasis
Gepants	Rimegepant, ubrogepant, zavegepant (nasal)	CGRP receptor antagonists; no vasoconstriction
Ditans	Lasmiditan	5-HT _{1F} agonist; no vasoconstriction; no driving for 8 h
Ergots	Dihydroergotamine	Status migrainosus, cluster

Prevention — for ≥ 4 migraine days a month, disability despite acute treatment, or acute-medication overuse.

Class	Drugs
β -blockers	Propranolol, metoprolol
Antiseizure medications	Topiramate; valproate (not in women of childbearing potential)
Antidepressants	Amitriptyline, venlafaxine
Others	Candesartan, flunarizine
CGRP monoclonal antibodies	Erenumab (receptor), fremanezumab, galcanezumab, eptinezumab (ligand; quarterly IV)
Gepants	Atogepant (daily), rimegepant (alternate days)
Botulinum toxin	OnabotulinumtoxinA — chronic migraine only (PREEMPT)

CGRP monoclonal antibodies. STRIVE (erenumab, episodic migraine, 2017): $\geq 50\%$ reduction in monthly migraine days in **43 %** (70 mg) and **50 %** (140 mg) vs 27 % with placebo. The European Headache Federation guideline (2022 update) recommends CGRP mAbs for episodic and chronic migraine; its 2023 consensus supports them as a first-line preventive option. Few interactions; watch constipation and hypertension with erenumab.

Tension-type headache

The commonest primary headache. ≥ 10 episodes of 30 min–7 days with ≥ 2 of: bilateral, pressing, mild–moderate, not aggravated by activity; no nausea; no more than one of photophobia or phonophobia.

Acute: simple analgesics, NSAIDs. Prevention: amitriptyline (best evidence), mirtazapine, venlafaxine. Physiotherapy, CBT, relaxation.

Trigeminal autonomic cephalalgias

	Cluster	Paroxysmal hemicrania	SUNCT/SUNA	Hemicrania continua
Duration	15–180 min	2–30 min	1–600 s	Continuous (> 3 months) with exacerbations
Frequency	Every other day to 8/day	> 5 /day	At least once daily, often many	Daily
Sex	M $>$ F	F $\geq$ M	M $\geq$ F	F $>$ M
Indomethacin	No response	Absolute	No response	Absolute

	Cluster	Paroxysmal hemicrania	SUNCT/SUNA	Hemicrania continua
Treatment	Oxygen, triptan; verapamil	Indomethacin	Lamotrigine, IV lidocaine	Indomethacin

All have ipsilateral autonomic features (lacrimation, injection, rhinorrhoea, ptosis, miosis, eyelid oedema, sweating) and/or restlessness.

Cluster headache — severe unilateral orbital or temporal pain with restlessness, circadian and circannual periodicity, often waking from sleep; alcohol triggers attacks during a bout.

Phase	Treatment
Acute	100 % oxygen 12–15 L/min by non-rebreather mask for 15 min; sumatriptan 6 mg SC; zolmitriptan nasal
Transitional	Greater occipital nerve block; short oral steroid course
Preventive	Verapamil (ECG before and during titration for heart block); lithium; topiramate; galcanezumab (episodic cluster, US)
Refractory	Non-invasive vagus nerve stimulation; occipital nerve stimulation

Secondary headaches

Idiopathic intracranial hypertension. Young women with obesity or recent weight gain; also tetracyclines, vitamin A derivatives, steroid withdrawal, lithium. Daily headache, pulsatile tinnitus, transient visual obscurations, diplopia from VI palsy; papilloedema and field loss (enlarged blind spot, inferonasal loss).

- Modified Dandy (Friedman 2013) criteria: papilloedema, normal examination apart from cranial nerves, normal parenchyma on MRI/MRV, normal CSF composition, opening pressure ≥ 25 cmH₂O (≥ 28 in children) in lateral decubitus.
- Rule out venous sinus thrombosis with MRV.
- Treatment: weight loss (bariatric surgery superior in IIH:WT 2021), acetazolamide, topiramate; GLP-1 agonists emerging. Fulminant or progressive visual loss: venous sinus stenting, CSF shunting, optic nerve sheath fenestration.

Giant cell arteritis. Age > 50 ; new headache, scalp tenderness, jaw claudication, polymyalgia, visual loss from arteritic anterior ischaemic optic neuropathy. ESR/CRP raised. Temporal artery ultrasound (halo sign) or biopsy; ACR/EULAR 2022 criteria. **Start steroids immediately** — prednisolone 40–60 mg, or IV methylprednisolone with visual loss; do not wait for biopsy (still positive for 2+ weeks). Tocilizumab is steroid-sparing (GiACTA).

Medication-overuse headache. Headache on ≥ 15 days/month in a patient with a pre-existing headache disorder, with overuse for > 3 months: triptans, ergots, opioids, combination analgesics on ≥ 10 days/month; simple analgesics on ≥ 15 days/month. Withdraw (abrupt except opioids, barbiturates, benzodiazepines) and start prevention at the same time.

Spontaneous intracranial hypotension. Orthostatic headache, often after a CSF leak or CSF–venous fistula. MRI: pachymeningeal enhancement, brain sagging, subdural collections, engorged venous sinuses, pituitary enlargement (SEEPS). Epidural blood patch; targeted repair.

Facial pain — trigeminal neuralgia

Paroxysms of electric-shock pain lasting a fraction of a second to 2 minutes in V2 and/or V3, triggered by light touch, chewing, talking, cold wind; refractory periods.

- **Classical** (neurovascular compression with morphological change), **secondary** (MS, tumour), **idiopathic**.
- MRI with high-resolution sequences in all; secondary causes suggested by age < 40 , bilateral pain, sensory loss.
- Treatment: carbamazepine or oxcarbazepine first line; lamotrigine, baclofen, gabapentin. Microvascular decompression for classical TN (best long-term results); percutaneous procedures or radiosurgery otherwise.

Pattern recognition — Chapter 7

Sign	Description	Condition
Empty (partially empty) sella	Flattened pituitary against the sellar floor	IIH
Posterior globe flattening	Flattened posterior sclera, optic disc protrusion	IIH
Distended optic nerve sheaths, tortuous optic nerves	Periopic CSF dilatation	IIH
Transverse sinus stenosis	Bilateral narrowing on MRV	IIH
Pachymeningeal enhancement, brain sagging	Diffuse dural enhancement, effaced cisterns, low tonsils	Spontaneous intracranial hypotension
Tram-track sign	Enhancing sheath around a non-enhancing optic nerve	Optic nerve sheath meningioma
Halo sign	Hypoechoic wall thickening on temporal artery ultrasound	Giant cell arteritis

Infections of the Nervous System

Key tables: CSF by meningitis type · Empirical antibiotics · HSV encephalitis · Autoimmune encephalitis · Prion disease · HIV

Syndromes	Meningitis, encephalitis, myelitis, abscess, prion disease
Tools	CSF (cells, protein, glucose ratio, Gram stain, culture, PCR, antigen), imaging, serology
Principle	Many CNS infections are emergencies: treat empirically while the work-up proceeds

Meningitis

Type	Common causes
Acute bacterial	<i>S. pneumoniae</i> , <i>N. meningitidis</i> ; <i>Listeria</i> (neonates, > 50, pregnancy, immunosuppression, alcohol); group B streptococcus and <i>E. coli</i> (neonates); <i>H. influenzae</i>
Viral	Enteroviruses (commonest), HSV-2 (recurrent — Mollaret), VZV, HIV seroconversion
Tuberculous	<i>M. tuberculosis</i> — basal meningitis, cranial neuropathies, hydrocephalus, infarcts
Fungal	<i>Cryptococcus</i> (HIV, transplant), <i>Coccidioides</i> , <i>Histoplasma</i> , <i>Candida</i>
Chronic	TB, fungi, syphilis, Lyme, <i>Brucella</i> , carcinomatous, sarcoid

CSF	Bacterial	Viral	TB / fungal
Opening pressure	Raised	Normal or mildly raised	Raised (very high in cryptococcal)
Appearance	Turbid	Clear	Clear, fibrin web (TB)
White cells	1000–5000, neutrophils	5–500, lymphocytes (early neutrophils possible)	50–500, lymphocytes
Glucose (CSF:serum)	< 0.4	Normal (> 0.6)	Low
Protein	High (> 1 g/L)	Normal or mildly raised	High (TB often > 1–5 g/L)
Gram stain	Positive in 60–90 % (less after antibiotics)	Negative	India ink; ZN stain insensitive
Specific tests	Culture, bacterial PCR	Enterovirus, HSV, VZV PCR	Cryptococcal antigen; TB culture, Xpert MTB/RIF Ultra; ADA

Empirical treatment of bacterial meningitis

Blood cultures, then **antibiotics and dexamethasone within an hour** — do not delay for CT or LP. CT first only with focal signs, papilloedema, new seizures, immunosuppression or GCS < 10.

Group	Regimen
< 1 month	Ampicillin + cefotaxime (or gentamicin)
1 month – 50 years	Ceftriaxone or cefotaxime (+ vancomycin or rifampicin where pneumococcal resistance is common)
> 50 years, immunosuppressed, alcohol, pregnancy	Add ampicillin/amoxicillin for <i>Listeria</i>
Post-neurosurgery, shunt, penetrating trauma	Vancomycin + cefepime, ceftazidime or meropenem

Dexamethasone 10 mg (0.15 mg/kg) every 6 h for 4 days, starting with or just before the first antibiotic dose — reduces death and hearing loss in pneumococcal meningitis (de Gans 2002). Stop if not bacterial. Chemoprophylaxis of close contacts of meningococcal disease (ciprofloxacin, rifampicin or ceftriaxone).

Encephalitis

Brain parenchymal inflammation: encephalopathy with fever, seizures, focal deficits, CSF pleocytosis or imaging/EEG changes.

Herpes simplex encephalitis. The commonest sporadic fatal encephalitis in Western countries; HSV-1 in adults (HSV-2 in neonates).

- Fever, confusion, behavioural change, aphasia, seizures.
- MRI: asymmetric T2/FLAIR and DWI change in the medial temporal lobes, insula, orbitofrontal cortex and cingulate; basal ganglia spared; haemorrhage later.
- EEG: lateralised periodic discharges (LPDs; formerly PLEDs) over the temporal lobe.
- CSF: lymphocytic pleocytosis, red cells, raised protein. HSV PCR > 95 % sensitive – may be negative in the first 72 h; repeat if suspicion remains.
- **Aciclovir 10 mg/kg IV every 8 h for 14–21 days**, started on suspicion. Without treatment mortality is ~70 %.
- About a quarter develop **NMDAR encephalitis** 2–6 weeks later (relapse with choreoathetosis in children, psychiatric features in adults).

Virus	Features
VZV	Vasculopathy (large or small vessels), cerebellitis in children, myelitis; may occur without rash; aciclovir
CMV	Immunosuppressed; ventriculoencephalitis, polyradiculitis; ganciclovir or foscarnet
Enteroviruses	Summer–autumn; usually mild; EV-71 rhombencephalitis and acute flaccid myelitis
Arboviruses	West Nile (flaccid paralysis), Japanese encephalitis (thalamic and basal ganglia lesions), tick-borne encephalitis (Europe), Zika
Rabies	Hydrophobia, aerophobia, autonomic instability; nearly always fatal once symptomatic; post-exposure prophylaxis
HIV	Seroconversion meningoencephalitis

Autoimmune encephalitis

Antibody	Features	Tumour association
NMDAR	Young women and children; psychiatric onset, seizures, orofacial dyskinesia, catatonia, autonomic instability, hypoventilation, reduced consciousness; CSF antibodies more sensitive than serum	Ovarian teratoma (~40 % in young women); post-HSV
LGII	Older men; faciobrachial dystonic seizures, hyponatraemia, amnesia	Rare
CASPR2	Neuromyotonia, Morvan syndrome (insomnia, dysautonomia, encephalopathy), neuropathic pain	Thymoma (Morvan)
GABA-B receptor	Limbic encephalitis with prominent seizures	Small-cell lung cancer (~50 %)
AMPA	Limbic encephalitis, psychiatric features	Thymoma, lung, breast (~60 %)
GABA-A receptor	Refractory seizures, multifocal cortical FLAIR lesions	Thymoma
DPPX	Weight loss and diarrhoea, hyperekplexia, CNS hyperexcitability	Lymphoma (uncommon)
IgLON5	Sleep disorder (NREM and REM parasomnia, stridor), bulbar dysfunction, gait	Not paraneoplastic; HLA-DRB1*10:01

Treatment. First line: IV methylprednisolone, IVIG or PLEX (often combined) – start early on clinical grounds (Graus 2016 criteria) without waiting for antibodies. Second line: rituximab, cyclophosphamide. Remove any tumour.

Brain abscess

- Sources: contiguous (sinusitis, otitis, dental), haematogenous (endocarditis, lung abscess, congenital heart disease with right-to-left shunt), trauma or surgery.
- Headache (commonest), fever (only ~50 %), focal deficit, seizures.
- MRI: ring-enhancing lesion, smooth thin T2-hypointense capsule, **restricted diffusion in the cavity**, oedema; ring thinner on the ventricular side (risk of intraventricular rupture).
- Often polymicrobial: streptococci (*S. anginosus* group), anaerobes, *S. aureus*, Gram-negatives; *Toxoplasma*, *Nocardia*, fungi in immunosuppression.
- Aspiration or excision for diagnosis and when > 2.5 cm, with mass effect or no response; antibiotics (e.g. ceftriaxone + metronidazole) for 6–8 weeks; early oral step-down is increasingly used in selected patients.

Neurosyphilis

Treponema pallidum. Can occur at any stage.

- Early: asymptomatic, meningitis, cranial neuropathies (VIII, VII, II), ocular and otosyphilis, meningovascular stroke (Heubner's arteritis).
- Late: general paresis (dementia, psychiatric change) and tabes dorsalis (lightning pains, sensory ataxia, Charcot joints, Argyll Robertson pupils — small, irregular, accommodate but do not react to light).
- Diagnosis: serum treponemal and non-treponemal tests; CSF pleocytosis, raised protein; CSF VDRL specific but insensitive; CSF FTA-ABS sensitive but not specific (negative result excludes).
- Treatment: aqueous benzylpenicillin 18–24 million units/day (3–4 MU every 4 h) for 10–14 days; ceftriaxone is an alternative.

Lyme neuroborreliosis

Borrelia burgdorferi sensu lato (*B. garinii* in Europe), *Ixodes* ticks.

- Early localised: erythema migrans.
- Early disseminated: lymphocytic meningitis, cranial neuritis (facial palsy, often bilateral), painful radiculoneuritis (Bannwarth syndrome), carditis.
- Late: encephalomyelitis, acrodermatitis chronica atrophicans with neuropathy.
- Diagnosis: serology plus intrathecal antibody index; CSF CXCL13.

Treatment. Oral doxycycline 200 mg/day for 14 days is as effective as IV ceftriaxone for meningitis, cranial neuritis and radiculitis (Ljøstad 2008; IDSA/AAN/ACR 2020, EAN 2010). **IV ceftriaxone** 2 g daily for 14–21 days for parenchymal brain or spinal cord disease (encephalitis, myelitis, vasculitis).

Prion disease

Rapidly progressive, fatal neurodegeneration from misfolded prion protein (PrP^{Sc}).

Form	Share	Features
Sporadic CJD	~85 %	Age 55–75; rapidly progressive dementia, myoclonus (startle-sensitive), cerebellar and visual signs (Heidenhain variant), pyramidal and extrapyramidal signs, akinetic mutism; median survival ~4–6 months
Genetic	10–15 %	<i>PRNP</i> mutations — familial CJD, Gerstmann–Sträussler–Scheinker, fatal familial insomnia
Acquired	< 1 %	Iatrogenic (dura mater grafts, growth hormone), variant CJD, kuru

Investigation. MRI DWI/FLAIR: cortical ribboning and/or caudate and putamen hyperintensity (most sensitive test); EEG: periodic sharp-wave complexes (~1 Hz; late, may be absent); CSF: **RT-QuIC** (sensitivity ~90 %,

specificity ~100 %), 14-3-3 and total tau (non-specific). No disease-modifying treatment.

Variant CJD. Bovine spongiform encephalopathy exposure; young adults; early psychiatric and painful sensory symptoms; slower course (~14 months); pulvinar (hockey-stick) sign; tonsil biopsy positive.

HIV and the nervous system

Category	Manifestations
Primary HIV	Seroconversion meningitis; HIV-associated neurocognitive disorder; vacuolar myelopathy; CSF escape
Opportunistic infections (CD4 < 200, mostly < 100)	Toxoplasmosis, cryptococcal meningitis, PML, CMV, TB, syphilis
Neoplasm	EBV-positive primary CNS lymphoma
Peripheral	Distal symmetric sensory polyneuropathy (HIV, older nucleoside drugs), AIDP/CIDP, CMV polyradiculitis, mononeuritis multiplex
Muscle	HIV myopathy, zidovudine myopathy

	Toxoplasmosis	Primary CNS lymphoma
Lesions	Multiple, ring-enhancing, basal ganglia and corticomedullary junction; eccentric target sign	Single or few; periventricular, corpus callosum; ring enhancement in AIDS
Thallium SPECT / FDG-PET	Low uptake	High uptake
CSF	—	EBV DNA PCR
Test	Empirical pyrimethamine–sulfadiazine; response in 2 weeks	Biopsy

Cryptococcal meningitis. Headache with very high opening pressure; CSF cryptococcal antigen. Induction with single high-dose liposomal amphotericin B plus flucytosine and fluconazole (AMBITION-cm 2022; WHO 2022); repeated LPs to control pressure; delay ART 4–6 weeks.

Progressive multifocal leukoencephalopathy. JC polyomavirus in immunosuppression (HIV, natalizumab, rituximab, haematological malignancy). Subacute focal deficits, hemianopia, cognitive decline, ataxia. MRI: asymmetric subcortical white-matter lesions involving U-fibres, no mass effect, usually no enhancement (enhancement suggests IRIS); a sharp border towards cortex; punctate "milky way" lesions in natalizumab PML. CSF JCV PCR; biopsy if negative. Treatment: restore immunity (ART; stop natalizumab ± PLEX). Watch for IRIS.

Pattern recognition — Chapter 8

Sign	Description	Condition
Asymmetric medial temporal and insular FLAIR/DWI change	Basal ganglia spared	HSV encephalitis
Cortical ribboning	Gyriform DWI hyperintensity, with or without caudate–putamen involvement	Sporadic CJD
Pulvinar / hockey-stick sign	Bilateral posterior and dorsomedial thalamic hyperintensity	Variant CJD
Ring enhancement with restricted diffusion in the centre	Smooth, thin capsule	Pyogenic abscess (metastasis and glioblastoma usually do not restrict centrally)
Eccentric target sign	Ring with an eccentric enhancing nodule	Toxoplasmosis
Non-enhancing subcortical U-fibre lesions	Asymmetric, no mass effect	PML
Basal meningeal enhancement with hydrocephalus and infarcts	—	Tuberculous meningitis

Sign	Description	Condition
Gelatinous pseudocysts	Dilated perivascular spaces in the basal ganglia	Cryptococcosis
Cysts with a scolex (dot)	Starry-sky appearance in many cysts	Neurocysticercosis

Neuro-oncology

Key tables: MRI differential of enhancing lesions · WHO CNS5 2021 gliomas · Glioblastoma treatment · Paraneoplastic antibodies

Classification	Primary (gliomas, meningiomas, pituitary, nerve sheath, lymphoma) vs metastatic
Frequency	Metastases outnumber primary tumours in adults; meningioma is the commonest primary tumour, glioblastoma the commonest malignant one
Approach	Clinical picture + MRI + tissue with integrated molecular diagnosis

Clinical presentation

- Headache (~50 %), classically worse in the morning or with Valsalva — but usually non-specific.
- Seizures (~25–30 %; most common with slow-growing cortical tumours — low-grade glioma, oligodendroglioma; IDH-mutant tumours are especially epileptogenic).
- Focal deficits by location; cognitive and personality change (frontal, callosal).
- Raised ICP: headache, vomiting, papilloedema, false-localising VI palsy, reduced consciousness.

MRI differential

Feature	Low-grade glioma	Glioblastoma	Metastasis	Abscess	Lymphoma (immunocompetent)
Enhancement	Little or none	Thick irregular ring around necrosis	Ring or nodular	Thin smooth ring	Homogeneous, solid
Oedema	Minimal	Marked, infiltrative	Marked, out of proportion to size	Moderate	Mild–moderate
DWI	Facilitated	Variable (necrosis facilitated)	Variable	Restricted cavity	Restricted solid tumour (high cellularity)
Location	Cortex/subcortical, frontal and insular	White matter, crosses corpus callosum (butterfly)	Grey–white junction, watershed	Any	Periventricular, deep grey, corpus callosum
Other	Calcification in oligodendroglioma; T2–FLAIR mismatch (IDH-mutant astrocytoma)	Haemorrhage, high rCBV	Multiple, high rCBV	Daughter lesions	Melts with steroids — hold steroids before biopsy

WHO CNS5 (2021) classification of adult diffuse gliomas

Diagnosis is now **integrated**: histology plus molecular markers. Grades are Arabic and assigned within each tumour type. "Anaplastic", "diffuse astrocytoma, IDH-wildtype" and "secondary glioblastoma" have been retired.

Tumour type	Defining molecular features	CNS WHO grade	Median survival (approx.)
Astrocytoma, IDH-mutant	IDH1/2 mutation, ATRX loss, TP53; no 1p/19q codeletion	2, 3 or 4 (grade 4 if necrosis/MVP or CDKN2A/B homozygous deletion)	Grade 2 > 10 years; grade 4 ~3 years
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	IDH mutation + 1p/19q codeletion; <i>TERT</i> promoter mutation	2 or 3	> 15 years (grade 2)

Tumour type	Defining molecular features	CNS WHO grade	Median survival (approx.)
Glioblastoma, IDH-wildtype	IDH-wildtype; necrosis or microvascular proliferation, or any of <i>TERT</i> promoter mutation, <i>EGFR</i> amplification, +7/-10	4	~15 months

Other types to know: pilocytic astrocytoma (CNS WHO grade 1; *BRAF-KIAA1549* fusion; cerebellar cyst with enhancing mural nodule in children); diffuse midline glioma, H3 K27-altered (grade 4; pons, thalamus, cord; children and young adults); pleomorphic xanthoastrocytoma (*BRAF V600E*).

Glioblastoma

- Commonest malignant primary brain tumour in adults; peak 55–75 years.
- *MGMT* promoter methylation predicts benefit from temozolomide and is a favourable prognostic marker.
- Standard: maximal safe resection, then radiotherapy 60 Gy in 30 fractions with daily temozolomide, then 6 cycles of adjuvant temozolomide (Stupp). Elderly or frail: hypofractionated RT (40 Gy/15) ± temozolomide (Perry 2017), or temozolomide alone if *MGMT*-methylated.
- Tumour-treating fields with adjuvant temozolomide prolonged survival (EF-14: 20.9 vs 16.0 months).
- Recurrence: re-resection, lomustine, bevacizumab (improves progression-free survival and steroid needs, not overall survival).

Stupp et al. (2005). Radiotherapy plus concurrent and adjuvant temozolomide versus radiotherapy alone: median survival 14.6 vs 12.1 months; 2-year survival 26.5 % vs 10.4 %. Benefit largest with *MGMT* methylation.

INDIGO (2023). Vorasidenib, an IDH1/2 inhibitor, more than doubled progression-free survival (27.7 vs 11.1 months) in residual or recurrent grade 2 IDH-mutant glioma after surgery only, and delayed the need for radiotherapy and chemotherapy.

Meningioma

- Commonest primary intracranial tumour; arachnoid cap cells; women; radiation exposure and NF2 are risk factors.
- CNS WHO grade 1 (~80 %), grade 2 atypical (~15–20 %; also brain invasion), grade 3 anaplastic (~1–3 %; also *TERT* promoter mutation or *CDKN2A/B* deletion).
- MRI: extra-axial, dural-based, homogeneous enhancement, **dural tail**, CSF cleft, hyperostosis, calcification.
- Observation if small and asymptomatic; surgery (Simpson grade predicts recurrence); radiotherapy or radiosurgery for residual, grade 2–3 or inoperable tumours.

Pituitary adenoma (pituitary neuroendocrine tumour)

- Functioning vs non-functioning; macroadenoma ≥ 10 mm.
- Prolactinoma is the commonest functioning tumour; others: GH (acromegaly), ACTH (Cushing's disease), TSH, gonadotroph (usually non-functioning).
- Bitemporal hemianopia, headache, hypopituitarism, apoplexy.
- Prolactinoma: dopamine agonists (cabergoline) first line, even for macroadenomas with visual loss. Others: transsphenoidal surgery, medical therapy, radiotherapy.

Metastases

- The commonest intracranial tumours in adults.

- Sources: lung (~50 %), breast (15–20 %), melanoma (highest propensity), renal, colorectal. Haemorrhagic: melanoma, renal, thyroid, choriocarcinoma.
- Grey–white junction and watershed zones; oedema out of proportion.
- Treatment: surgery for a single accessible lesion or diagnosis; stereotactic radiosurgery for limited (and increasingly multiple) lesions; whole-brain radiotherapy with memantine and hippocampal avoidance when needed; targeted therapy and immunotherapy (EGFR, ALK, BRAF, checkpoint inhibitors) have intracranial activity.

Primary CNS lymphoma

Diffuse large B-cell lymphoma confined to the brain, eyes, CSF or cord. Immunocompetent older adults, or EBV-driven in immunosuppression. Homogeneous enhancement, restricted diffusion, periventricular and callosal; vitreoretinal involvement in ~20 % (slit-lamp examination). Stereotactic biopsy **before steroids**. High-dose methotrexate-based chemotherapy, then consolidation (autologous stem-cell transplant or whole-brain RT).

Paraneoplastic neurological syndromes

PNS-Care updated criteria (Graus 2021) classify antibodies by cancer risk.

Risk	Antibody	Syndrome	Usual cancer
High (> 70 %)	Hu (ANNA-1)	Sensory neuronopathy, encephalomyelitis, limbic encephalitis, GI dysmotility	Small-cell lung cancer
High	Yo (PCA-1)	Cerebellar degeneration	Ovary, breast
High	Ri (ANNA-2)	Brainstem encephalitis, opsoclonus–myoclonus, jaw dystonia	Breast, SCLC
High	CV2/CRMP5	Encephalomyelitis, chorea, optic neuropathy, neuropathy	SCLC, thymoma
High	Ma2	Limbic, diencephalic and brainstem encephalitis (hypersomnia, vertical gaze palsy)	Testicular germ-cell tumour
High	Amphiphysin	Stiff-person syndrome, neuropathy	Breast, SCLC
High	Tr (DNER)	Cerebellar degeneration	Hodgkin lymphoma
High	KLHL11	Rhombencephalitis	Testicular seminoma
Intermediate	AMPA, GABA-B, mGluR5, P/Q VGCC, NMDAR	Encephalitis; LEMS (VGCC)	Thymoma, SCLC, Hodgkin, ovarian teratoma
Low (< 30 %)	LGI1, CASPR2, GAD65, AChR, GlyR	Limbic encephalitis, Morvan, stiff-person, MG	Usually none (thymoma for CASPR2–Morvan)

Stiff-person syndrome with GAD65 antibodies is usually autoimmune, not paraneoplastic (associations: type 1 diabetes, thyroiditis). Amphiphysin-positive SPS points to breast cancer. **Opsoclonus–myoclonus** in children: neuroblastoma (usually no antibody); in adults: SCLC, breast, teratoma.

Pattern recognition — Chapter 9

Sign	Description	Condition
Dural tail	Enhancing dura tapering from an extra-axial mass	Meningioma
Butterfly glioma	Enhancing mass crossing the corpus callosum	Glioblastoma, lymphoma
T2–FLAIR mismatch	Homogeneous T2 hyperintensity with relatively hypointense FLAIR centre and bright rim	Astrocytoma, IDH-mutant, 1p/19q intact

Sign	Description	Condition
Homogeneous periventricular enhancement with restricted diffusion	Lesion shrinks after steroids	Primary CNS lymphoma
Cyst with enhancing mural nodule	Well-circumscribed	Pilocytic astrocytoma (children); haemangioblastoma (adults, von Hippel-Lindau)
Calcified cortical mass	Frontal, gyriform calcification	Oligodendroglioma
Snowball lesions	Central corpus callosum lesions	Susac syndrome (not lymphoma)

Dementia and Cognitive Disorders

Key tables: Alzheimer's biomarkers · Anti-amyloid antibodies · McKeith 2017 DLB criteria · FTD variants · Reversible causes

Definition	Acquired decline in ≥ 1 cognitive domain sufficient to impair independence (major neurocognitive disorder)
Prevalence	~55 million worldwide; doubles about every 5 years after 65
Causes	Alzheimer's (60–70 %), vascular and mixed (15–20 %), Lewy body (5–10 %), frontotemporal (~5 %)
Under 65	Alzheimer's is still the commonest cause; FTD is second

Alzheimer's disease

Extracellular amyloid- β plaques and intracellular tau neurofibrillary tangles, beginning in the entorhinal cortex and hippocampus (Braak staging).

Stage	Features
Preclinical	Biomarkers abnormal, no symptoms
MCI due to AD	Objective impairment, independence preserved
Mild dementia	Episodic memory loss, word-finding, executive problems; mostly independent
Moderate	Disorientation, behavioural change, needs help with daily activities, wandering, sundowning
Severe	Loss of language, incontinence, immobility, dysphagia

Atypical presentations: posterior cortical atrophy (visuospatial, Balint and Gerstmann features), logopenic aphasia, frontal (dysexecutive) variant.

Biomarker	Finding in AD
CSF	Low A β 42 (or A β 42/40 ratio), raised p-tau181 and total tau
Plasma	p-tau217 — accuracy close to CSF and PET; increasingly used in practice
Amyloid PET	Increased cortical uptake
Tau PET	Neocortical uptake tracking symptoms
FDG-PET	Temporoparietal and posterior cingulate hypometabolism
MRI	Hippocampal and medial temporal atrophy (MTA score)
Genetics	APOE ϵ 4 risk (one copy ~3 $\times$, two copies ~8–12 $\times$); autosomal dominant <i>APP</i> , <i>PSEN1</i> , <i>PSEN2</i> ; Down syndrome

The Alzheimer's Association **2024 revised criteria** define AD biologically by core biomarkers (amyloid plus tau), separately from clinical staging; the IWG (2024) still requires a clinical syndrome for diagnosis. Know that the two frameworks differ.

Treatment

Class	Drugs	Use
Cholinesterase inhibitors	Donepezil, rivastigmine (also patch), galantamine	Mild–moderate (and severe) AD; bradycardia, syncope, GI effects, vivid dreams
NMDA antagonist	Memantine	Moderate–severe AD
Anti-amyloid antibodies	Lecanemab, donanemab	Early symptomatic AD (MCI or mild dementia) with confirmed amyloid

Anti-amyloid antibodies. Clarity AD (lecanemab, 2023): 27 % slower decline on CDR-SB at 18 months. TRAILBLAZER-ALZ 2 (donanemab, 2023): 35 % slower decline on iADRS in low/medium tau; dosing stops once amyloid clears. Main risk: **ARIA** (oedema ARIA-E, haemorrhage ARIA-H), highest in *APOE* ε4 homozygotes; MRI monitoring; avoid with anticoagulation. Both are licensed in the US; in the EU both are approved only for patients who are not ε4 homozygotes. **Aducanumab was withdrawn by its maker in 2024.**

Lewy body dementia

Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) — the **one-year rule**: dementia before or within a year of parkinsonism = DLB; dementia after more than a year of established PD = PDD.

McKeith 2017 criteria

Essential: dementia (memory may be relatively preserved early; attention, executive and visuospatial deficits prominent).

Core clinical features 1. Fluctuating cognition with pronounced variations in attention and alertness 2. Recurrent, well-formed visual hallucinations 3. REM sleep behaviour disorder (may precede cognitive decline by years) 4. One or more spontaneous cardinal features of parkinsonism

Indicative biomarkers - Reduced dopamine transporter uptake in the basal ganglia (DaT-SPECT or PET) - Low uptake on ¹²³I-MIBG myocardial scintigraphy - Polysomnographic confirmation of REM sleep without atonia

Supportive clinical features: severe sensitivity to antipsychotics, postural instability, repeated falls, syncope, severe autonomic dysfunction, hypersomnia, hyposmia, other hallucinations, systematised delusions, apathy, anxiety, depression. **Supportive biomarkers:** relative preservation of medial temporal lobes; occipital hypoperfusion/hypometabolism with the cingulate island sign; posterior slow-wave EEG activity.

Category	Requirement
Probable DLB	≥ 2 core features (with or without biomarkers), or 1 core feature + ≥ 1 indicative biomarker
Possible DLB	1 core feature without indicative biomarkers, or ≥ 1 indicative biomarker without core features

Supportive features do **not** establish possible DLB on their own. Probable DLB should not be diagnosed on biomarkers alone.

Treatment. Cholinesterase inhibitors first line (rivastigmine, donepezil) — help cognition, fluctuations and hallucinations; memantine adjunct; low-dose levodopa for parkinsonism; melatonin or clonazepam for RBD; midodrine, fludrocortisone or droxidopa for orthostatic hypotension.

Neuroleptic sensitivity. Up to half of patients with DLB react severely to antipsychotics — rigidity, sedation, autonomic instability, a neuroleptic malignant-like syndrome and increased mortality. Avoid typical antipsychotics and risperidone, olanzapine and haloperidol. If unavoidable: low-dose quetiapine or clozapine (pimavanserin where available), with close monitoring.

Vascular cognitive impairment

The second commonest cause of dementia; often mixed with AD.

Type	Description
Multi-infarct	Several cortical infarcts; stepwise decline
Strategic infarct	Single infarct in thalamus, angular gyrus, caudate, basal forebrain, genu of internal capsule
Subcortical small-vessel disease	White-matter hyperintensities and lacunes; gradual decline — the commonest form

Type	Description
CADASIL	<i>NOTCH3</i> ; migraine with aura, strokes, mood disorder; anterior temporal pole and external capsule white-matter change
Mixed	Vascular plus Alzheimer's pathology

Features: slowed processing and executive dysfunction more than memory; early gait disturbance and urinary symptoms; pseudobulbar signs. Treat vascular risk factors.

Frontotemporal dementia

Second commonest dementia under 65. Up to 40 % familial: *C9orf72*, *GRN*, *MAPT*.

Variant	Features	Usual pathology
Behavioural variant (bvFTD)	Disinhibition, apathy, loss of empathy, compulsive behaviour, hyperorality and sweet craving, executive dysfunction (Rascovsky 2011: ≥ 3 of 6 for possible)	Tau, TDP-43 or FUS
Non-fluent/agrammatic PPA	Effortful speech, agrammatism, apraxia of speech; left inferior frontal–insular atrophy	Tau (4R)
Semantic variant PPA	Loss of word and object meaning, anomia, surface dyslexia; anterior temporal atrophy (left > right)	TDP-43 type C
Logopenic variant PPA	Word-finding pauses, impaired repetition of sentences, phonological errors; left temporoparietal atrophy	Usually Alzheimer's disease
FTD-ALS	bvFTD with motor neuron disease	TDP-43 (<i>C9orf72</i>)

No disease-modifying therapy; SSRIs or trazodone for behaviour; avoid cholinesterase inhibitors (may worsen behaviour).

Normal-pressure hydrocephalus

Triad: magnetic gait apraxia (earliest and most responsive), urinary urgency/incontinence, subcortical cognitive decline. MRI: ventriculomegaly (Evans index > 0.3), **DESH** (disproportionately enlarged subarachnoid-space hydrocephalus – tight high convexity sulci with enlarged Sylvian fissures), callosal angle < 90°. High-volume tap test or lumbar drain; ventriculoperitoneal shunt.

Reversible and treatable contributors

- Drugs: anticholinergics, benzodiazepines, opioids, sedatives.
- Metabolic: hypothyroidism, B12 or thiamine deficiency, hyponatraemia, hypercalcaemia, hepatic or renal failure.
- Infection: syphilis, HIV, chronic meningitis.
- Structural: chronic subdural haematoma, NPH, tumour.
- Immune: autoimmune encephalitis, Hashimoto's encephalopathy (SREAT).
- Psychiatric: depression.
- Sleep: obstructive sleep apnoea.

Pattern recognition — Chapter 10

Sign	Description	Condition
Medial temporal atrophy	Hippocampal volume loss (MTA score ≥ 2 under 75)	Alzheimer's disease

Sign	Description	Condition
Posterior cingulate/precuneus hypometabolism	FDG-PET	Alzheimer's disease
Knife-edge atrophy	Severe frontal and/or anterior temporal atrophy	FTD (semantic variant: anterior temporal pole)
Cingulate island sign	Preserved posterior cingulate metabolism with occipital hypometabolism	DLB
Abnormal DaT-SPECT	Reduced striatal uptake ("full stop" instead of "comma")	DLB, PD, atypical parkinsonism — normal in AD
White-matter hyperintensities, lacunes	Periventricular and deep	Small-vessel disease
Anterior temporal and external capsule hyperintensity	Young patient with migraine and strokes	CADASIL
DESH, narrow callosal angle	Ventriculomegaly out of proportion to atrophy	Normal-pressure hydrocephalus

Sleep Disorders

Key tables: Sleep stages · Insomnia and CBT-I · Obstructive sleep apnoea · Narcolepsy (ICSD-3) · Restless legs · Parasomnias

Classification (ICSD-3-TR)	Insomnia, sleep-related breathing disorders, central hypersomnolence, circadian rhythm disorders, parasomnias, sleep-related movement disorders
Evaluation	History from patient and bed partner, sleep diary, Epworth Sleepiness Scale, actigraphy, polysomnography, MSLT

Sleep architecture

Stage	Features	Share of night (adult)
N1	Theta, vertex waves, slow rolling eye movements, hypnic jerks	~5 %
N2	Sleep spindles, K-complexes	45–55 %
N3	Slow-wave (delta) sleep; mostly in the first third of the night	15–20 %
REM	Desynchronised EEG, rapid eye movements, muscle atonia, dreaming; longer towards morning	20–25 %

NREM parasomnias arise from N3 early in the night; REM parasomnias later in the night.

Insomnia

Difficulty initiating or maintaining sleep, or early waking, despite adequate opportunity, with daytime impairment.

Chronic insomnia: ≥ 3 nights a week for ≥ 3 months.

CBT-I is first line (ESRS 2023, AASM): sleep restriction, stimulus control, cognitive therapy, relaxation, sleep hygiene education. More durable than drugs. Short-term pharmacotherapy when CBT-I is unavailable or insufficient: Z-drugs, low-dose doxepin, dual orexin receptor antagonists (daridorexant, lemborexant, suvorexant); prolonged-release melatonin over 55.

Obstructive sleep apnoea

Recurrent upper-airway collapse in sleep causing apnoeas and hypopnoeas, desaturation and arousals. AHI: mild 5–14, moderate 15–29, severe ≥ 30 events/hour.

Risk factors. Obesity, large neck (> 43 cm men, > 40 cm women), male sex, post-menopause, retrognathia, tonsillar hypertrophy, macroglossia, alcohol and sedatives. STOP-BANG for screening.

Treatment	Indication	Notes
CPAP	Moderate–severe, or symptomatic mild	Most effective; adherence is the limitation
Mandibular advancement device	Mild–moderate or CPAP-intolerant	
Weight loss	All overweight patients	Includes GLP-1/GIP agonists — tirzepatide approved for OSA with obesity (SURMOUNT-OSA 2024)
Positional therapy	Supine-predominant OSA	
Hypoglossal nerve stimulation	Moderate–severe, CPAP-intolerant, without complete concentric palatal collapse; BMI limit varies by label	
Surgery	Selected anatomy	Tonsillectomy (children), maxillomandibular advancement

Treatment	Indication	Notes
Avoid alcohol and sedatives	All	

Central sleep apnoea: heart failure (Cheyne–Stokes), opioids, brainstem lesions, Chiari malformation, high altitude.

Narcolepsy (ICSD-3)

	Narcolepsy type 1	Narcolepsy type 2
Daytime sleepiness	Daily for ≥ 3 months	Daily for ≥ 3 months
Plus	Cataplexy with positive MSLT/PSG, or CSF hypocretin-1 ≤ 110 pg/mL (or $< \frac{1}{3}$ of normal)	No cataplexy, CSF hypocretin normal or not measured
MSLT	Mean sleep latency ≤ 8 min and ≥ 2 SOREMPs (a SOREMP on the preceding night's PSG counts as one)	Same
Pathology	Loss of hypothalamic hypocretin (orexin) neurons; HLA-DQB1*06:02 in $> 95\%$	Heterogeneous

Cataplexy: brief bilateral loss of muscle tone with preserved consciousness, triggered by emotion (laughter, surprise); facial and neck involvement common in children. Other features: sleep paralysis, hypnagogic and hypnopompic hallucinations, fragmented night sleep, automatic behaviour.

Symptom	Treatment
Sleepiness	Modafinil/armodafinil, pitolisant (H3 inverse agonist), solriamfetol (DNRI), sodium oxybate; methylphenidate and amphetamines second line; scheduled naps
Cataplexy	Sodium oxybate (including low-sodium and once-nightly forms), pitolisant, venlafaxine, SSRIs, clomipramine
Disturbed night sleep	Sodium oxybate

Idiopathic hypersomnia: sleepiness with long unrefreshing sleep and sleep inertia, MSLT ≤ 8 min with < 2 SOREMPs, or ≥ 11 h total sleep on 24-hour PSG.

Restless legs syndrome (Willis–Ekbom disease)

IRLSSG essential criteria (URGE): - **Urge** to move the legs, usually with unpleasant sensations - **R**est induces or worsens it - **G**ets better with movement - **E**vening and night worsening - Not explained by another condition (cramps, positional discomfort, myalgia, oedema, arthritis)

Associations: iron deficiency, renal failure, pregnancy, neuropathy, drugs (antidepressants except bupropion, antihistamines, dopamine antagonists). ~80 % have periodic limb movements of sleep.

AASM clinical practice guideline (2024).

- **Iron:** check ferritin and transferrin saturation. Treat if ferritin $\leq 75 \mu\text{g/L}$ or TSAT $< 20 \%$ — oral ferrous sulfate, or IV ferric carboxymaltose (strong recommendation), low-molecular-weight iron dextran or ferumoxytol.
- **First-line drugs: $\alpha 2\delta$ ligands** — gabapentin enacarbil, gabapentin, pregabalin (strong recommendation).
- **Dopamine agonists (pramipexole, ropinirole, rotigotine): standard use is no longer recommended** because of **augmentation** (earlier onset, greater intensity, spread to arms). Short-term use may be appropriate in selected patients who accept the risk.
- Others: extended-release oxycodone or low-dose opioids for refractory RLS; dipyrindamole; bilateral high-frequency peroneal nerve stimulation.
- Managing augmentation: correct iron, switch to an $\alpha 2\delta$ ligand or opioid, then slowly taper the dopamine agonist.

Parasomnias

	NREM parasomnia (arousal disorder)	REM sleep behaviour disorder
Examples	Sleepwalking, sleep terrors, confusional arousals	Dream-enactment behaviour
Timing	First third of the night	Second half of the night
Age	Children, young adults	Men over 50
Recall	Little or none	Vivid dream recall; wakes quickly and is oriented
PSG	Arousals from N3	REM sleep without atonia — required for diagnosis
Significance	Usually benign	> 70–90 % develop an α-synucleinopathy (PD, DLB, MSA) over 10–15 years
Treatment	Safety, sleep hygiene, treat triggers	Bedroom safety; melatonin first, clonazepam

Pattern recognition — Chapter 11

Sign	Description	Condition
Chiari I malformation	Peg-like tonsils ≥ 5 mm below the foramen magnum	Cough headache, central and obstructive sleep apnoea, syringomyelia
Hypothalamic lesion with hypersomnia	Bilateral hypothalamic signal	Secondary narcolepsy (Ma2 encephalitis, NMOSD, sarcoid, tumour)
REM sleep without atonia	Tonic or phasic chin/limb EMG during REM	RBD — prodromal synucleinopathy

Autonomic Disorders

Key tables: Autonomic testing · Orthostatic hypotension · POTS · Horner's syndrome localisation · Neurogenic bladder

Divisions	Sympathetic (thoracolumbar T1–L2) and parasympathetic (craniosacral — III, VII, IX, X and S2–S4)
Functions	Cardiovascular, thermoregulatory, gastrointestinal, urogenital, pupillary, secretomotor
Approach	History, lying and standing BP and HR, autonomic testing, find the cause

Autonomic testing

Test	What it measures
Heart-rate variability to deep breathing	Cardiovagal (parasympathetic) function
Valsalva ratio and BP phases	Cardiovagal and adrenergic function (absent phase IV overshoot and prolonged phase II in adrenergic failure)
Head-up tilt	Orthostatic hypotension, POTS, vasovagal syncope
QSART, sudomotor tests, thermoregulatory sweat test	Postganglionic (QSART) and pre- plus postganglionic (TST) sudomotor function
Supine and standing plasma noradrenaline	Low supine noradrenaline in postganglionic failure (PD, PAF); normal supine in MSA
Cardiac MIBG	Postganglionic sympathetic denervation (PD, DLB, PAF) — normal in MSA
Skin biopsy	Small-fibre density; phosphorylated α -synuclein deposits

Orthostatic hypotension

Sustained fall in systolic BP ≥ 20 mmHg or diastolic ≥ 10 mmHg within 3 minutes of standing or head-up tilt ($\geq 30/15$ mmHg if supine hypertension). **Neurogenic OH:** inadequate heart-rate rise — $\Delta\text{HR}/\Delta\text{SBP} < 0.5$ bpm/mmHg.

Causes: α -synucleinopathies (PD, DLB, MSA, pure autonomic failure), autonomic neuropathies (diabetes, amyloid, autoimmune autonomic ganglionopathy with ganglionic AChR antibodies), drugs, hypovolaemia.

Non-drug measures. Head of bed raised 10–20° (reduces supine hypertension and nocturnal natriuresis); rise in stages; counter-maneuvres (leg crossing, squatting, muscle tensing); waist-high compression or abdominal binder; 2–3 L fluid and 6–10 g salt daily; 500 mL water bolus before standing; small, low-carbohydrate meals; avoid heat and alcohol; review culprit drugs.

Drug	Mechanism	Notes
Midodrine	$\alpha 1$ agonist	2.5–10 mg three times daily while upright; last dose ≥ 4 h before bed (supine hypertension), urinary retention, piloerection
Droxidopa	Noradrenaline precursor	Licensed for neurogenic OH (US); supine hypertension
Fludrocortisone	Mineralocorticoid — volume expansion	Hypokalaemia, oedema, supine hypertension, heart failure
Pyridostigmine	Enhances ganglionic transmission	Modest effect; little supine hypertension
Atomoxetine	Noradrenaline reuptake inhibitor	Works when postganglionic fibres are preserved (e.g. MSA)

Postural orthostatic tachycardia syndrome

- Sustained heart-rate rise ≥ 30 bpm within 10 minutes of standing or tilt (≥ 40 bpm at age 12–19), usually to > 120 bpm.
- **No** orthostatic hypotension.
- Orthostatic intolerance symptoms for ≥ 3 months.
- Not explained by dehydration, drugs, anaemia, hyperthyroidism, prolonged bed rest or another cause.

Mostly young women; often after viral infection (including COVID-19), with joint hypermobility or deconditioning. Treatment: fluids and salt, compression, graded recumbent exercise; then propranolol (low dose), ivabradine, midodrine, fludrocortisone, pyridostigmine.

Horner's syndrome

Ptosis (mild), miosis with dilation lag, apparent enophthalmos, facial anhidrosis (depends on level). Confirm with apraclonidine (reversal of anisocoria) or cocaine drops (failure of the affected pupil to dilate).

Neuron	Pathway	Causes	Anhidrosis
First order (central)	Hypothalamus $\rightarrow$ brainstem $\rightarrow$ ciliospinal centre (C8–T2)	Lateral medullary infarct, MS, syrinx, cervical cord lesion	Ipsilateral half of body
Second order (preganglionic)	C8–T2 $\rightarrow$ lung apex $\rightarrow$ superior cervical ganglion	Pancoast tumour , cervical rib, neck or thoracic surgery, neuroblastoma (children)	Face
Third order (postganglionic)	Superior cervical ganglion $\rightarrow$ along ICA $\rightarrow$ cavernous sinus $\rightarrow$ eye	Carotid dissection , cavernous sinus lesion, cluster headache	None or medial forehead only

Hydroxyamphetamine dilates a first- or second-order Horner pupil but not a third-order one. **Painful acute Horner's = carotid dissection until proven otherwise.**

Neurogenic bladder

Lesion	Bladder	Features
Suprapontine (stroke, dementia, frontal lesion, NPH)	Detrusor overactivity, coordinated sphincter	Urgency, urge incontinence; complete emptying
Spinal cord, between pons and sacral cord (MS, SCI)	Detrusor overactivity with detrusor-sphincter dyssynergia	Urgency, incomplete emptying, high pressure — upper-tract risk
Sacral cord, cauda equina, pelvic nerves	Underactive (areflexic) detrusor	Retention with overflow, saddle anaesthesia

Treatment: antimuscarinics or mirabegron for overactivity; intravesical botulinum toxin; clean intermittent self-catheterisation when post-void residual > 100 mL; tibial or sacral neuromodulation.

Pattern recognition — Chapter 12

Sign	Description	Condition
Apical lung mass	Superior sulcus tumour	Pancoast — second-order (preganglionic) Horner's
Crescentic intramural haematoma	T1 fat-saturated hyperintense crescent around a narrowed ICA	Carotid dissection — third-order (postganglionic) Horner's
Lateral medullary infarct	DWI lesion in the lateral medulla	Wallenberg — first-order (central) Horner's

Neuro-ophthalmology and Neuro-otology

Key tables: Visual field localisation · Ocular motor palsies · Pupils · Optic neuropathies · Peripheral vs central vertigo · HINTS · Nystagmus

Visual fields

Defect	Localisation
Monocular loss	Eye or optic nerve
Central or caecocentral scotoma	Optic nerve (optic neuritis, toxic-nutritional, LHON)
Junctional scotoma	Optic nerve–chiasm junction: ipsilateral central loss + contralateral superotemporal defect
Bitemporal hemianopia	Chiasm — pituitary adenoma (superior first), craniopharyngioma (inferior first)
Incongruous homonymous hemianopia	Optic tract, lateral geniculate body
Superior homonymous quadrantanopia ("pie in the sky")	Temporal lobe — Meyer's loop
Inferior homonymous quadrantanopia ("pie on the floor")	Parietal lobe
Congruous homonymous hemianopia with macular sparing	Occipital cortex (PCA infarct; macula has dual MCA/PCA supply)
Bilateral cortical blindness with denial (Anton's syndrome)	Bilateral occipital lobes

Ocular motor nerve palsies

Nerve	Findings	Key causes
III	Ptosis, eye down and out, dilated pupil when compressive	Pupil-involving: posterior communicating artery aneurysm (emergency CTA), uncal herniation. Pupil-sparing complete palsy: microvascular (diabetes, hypertension) — still image if age < 50, partial palsy or no recovery in 3 months
IV	Vertical diplopia worse on looking down and in; head tilt away from the affected side (Bielschowsky positive on tilt towards it)	Trauma (commonest), congenital decompensated, microvascular
VI	Horizontal diplopia worse on looking to the affected side and at distance	Raised ICP (false-localising), microvascular, petrous apex (Gradenigo), cavernous sinus, Wernicke's

Cavernous sinus: III, IV, V1, V2 and VI with Horner's; pituitary apoplexy, carotid–cavernous fistula, thrombosis, Tolosa–Hunt.

Internuclear ophthalmoplegia. Medial longitudinal fasciculus lesion: impaired adduction on the side of the lesion, abducting nystagmus of the other eye, preserved convergence. Bilateral in young adults → MS; unilateral in older adults → stroke. One-and-a-half syndrome: PPRF or VI nucleus plus MLF.

Pupils

Pupil	Features	Cause
Relative afferent pupillary defect	Paradoxical dilation on swinging light to the affected eye	Optic nerve or extensive retinal disease
Adie's tonic pupil	Large, poor light reaction, slow tonic near reaction; supersensitive to dilute pilocarpine 0.1 %	Ciliary ganglion; with areflexia = Holmes-Adie
Argyll Robertson	Small, irregular, light-near dissociation	Neurosyphilis (also diabetes)
Horner's	Small, dilation lag, ptosis	Sympathetic pathway (Chapter 12)
Pharmacological mydriasis	Fixed, large; no constriction with 1 % pilocarpine	Anticholinergic drops, scopolamine patches

Optic neuropathies

	Typical (MS) optic neuritis	Non-arteritic AION	Arteritic AION (GCA)	LHON
Age	20–45	> 50	> 70	Young men
Pain	On eye movement (> 90 %)	Usually none	Headache, jaw claudication	None
Disc	Normal (retrobulbar) or mildly swollen	Sectoral swelling, "disc at risk" (small cup)	Pallid ("chalky white") swelling	Hyperaemic, telangiectasia, no leakage
Field	Central scotoma	Altitudinal (inferior)	Altitudinal, severe	Central, then other eye within weeks
Course	Recovery over weeks	Little recovery	Risk to other eye — urgent steroids	Poor; idebenone

Optic Neuritis Treatment Trial: IV methylprednisolone speeds recovery without changing final acuity; oral prednisone alone at standard dose increased recurrence. Atypical features (bilateral, severe, painless, no recovery by 3 weeks, marked disc swelling) → NMOSD, MOGAD, sarcoid, infection.

Neuro-otology

Peripheral vs central acute vestibular syndrome

Feature	Peripheral	Central
Nystagmus	Unidirectional, horizontal-torsional, beats away from the lesion, suppressed by fixation, increases in gaze towards the fast phase (Alexander's law)	Direction-changing on lateral gaze, pure vertical or pure torsional, not suppressed by fixation
Head impulse test	Abnormal (corrective saccade)	Normal
Skew deviation	Absent	May be present
Gait	Can walk, falls towards the lesion	Often cannot stand unaided
Hearing	May be affected (labyrinthitis)	Usually spared — except AICA infarction , which can cause acute hearing loss with vertigo
Other signs	None	Diplopia, dysarthria, ataxia, weakness, numbness

HINTS (Head Impulse, Nystagmus, Test of Skew) in continuous acute vertigo with nystagmus: **any** of a normal head impulse, direction-changing nystagmus or skew deviation suggests stroke ("INFARCT"). HINTS-plus adds

new hearing loss. In expert hands more sensitive than early MRI-DWI, which misses ~10–20 % of posterior circulation strokes in the first 48 h.

Benign paroxysmal positional vertigo

- Commonest cause of vertigo; canalithiasis (free otoconia) or cupulolithiasis.
- Posterior canal ~80–90 %, horizontal ~10 %, anterior rare.
- Brief vertigo (< 1 min) with head position change.
- Posterior canal: Dix–Hallpike → upbeating torsional nystagmus towards the lowermost ear after a short latency, fatiguing. Treat with the Epley (or Semont) manoeuvre.
- Horizontal canal: supine roll test → geotropic or apogeotropic horizontal nystagmus; barbecue (Lempert) roll or Gufoni manoeuvre.

Other causes of vertigo

Condition	Features
Vestibular neuritis	Acute continuous vertigo for days, abnormal head impulse, no hearing loss; early steroids may aid recovery; vestibular rehabilitation
Ménière's disease	Episodes of 20 min–12 h with fluctuating low-frequency hearing loss, tinnitus, aural fullness
Vestibular migraine	Episodes of minutes to 72 h, migraine history and features with ≥ 50 % of episodes
Persistent postural-perceptual dizziness	Chronic non-spinning dizziness ≥ 3 months, worse upright and with visual motion
Vestibular paroxysmia	Seconds-long attacks, many a day, responds to carbamazepine

Nystagmus localisation

Nystagmus	Localisation
Downbeat	Cervicomedullary junction, flocculus — Chiari, cerebellar degeneration, lithium, Wernicke's, anti-GAD
Upbeat	Medulla or midbrain, cerebellar vermis; Wernicke's
Periodic alternating	Nodulus/uvula; responds to baclofen
See-saw	Parasellar (chiasm) or midbrain
Convergence–retraction	Dorsal midbrain (Parinaud) — pineal tumour, hydrocephalus
Gaze-evoked	Cerebellum, drugs (alcohol, antiseizure medications)
Pendular	MS, oculopalatal tremor (after Guillain–Mollaret triangle lesions)

Pattern recognition — Chapter 13

Sign	Description	Condition
Optic nerve enhancement	Short anterior segment (MS); long segment or chiasmal (NMOSD); perineural sheath (MOGAD)	Optic neuritis
Empty delta sign	Contrast-enhanced filling defect in the superior sagittal sinus	Cerebral venous sinus thrombosis
Cerebellopontine angle mass extending into the internal auditory canal ("ice-cream cone")	No dural tail; cystic change common	Vestibular schwannoma
CPA mass with dural tail, broad dural base, obtuse angle	Little IAC extension	Meningioma
Bilateral vestibular schwannomas	—	Neurofibromatosis type 2 (NF2-related schwannomatosis)
Restricted diffusion in a CPA lesion	Lobulated, insinuating	Epidermoid cyst

Neurological Complications of Systemic Disease

Key tables: Metabolic encephalopathies · Thyroid · Nutritional deficiencies · Drug-induced disorders · ICU-acquired weakness

Metabolic encephalopathies

Condition	Features	Points
Hepatic encephalopathy	Confusion, asterixis, triphasic waves; bilateral pallidal T1 hyperintensity (manganese)	Lactulose and rifaximin; look for precipitants (bleeding, infection, sedatives, constipation)
Uraemic encephalopathy	Confusion, asterixis, multifocal myoclonus, seizures	Dialysis; dialysis disequilibrium syndrome
Hyponatraemia	Confusion, seizures	Correct chronic hyponatraemia by $\leq 8-10$ mmol/L in 24 h to avoid osmotic demyelination
Osmotic demyelination	Days after rapid correction: dysarthria, dysphagia, quadriparesis, locked-in	Central pontine "trident" lesion, extrapontine (basal ganglia) involvement
Hypoglycaemia	Confusion, seizures, focal deficits	Restricted diffusion in cortex, hippocampi, basal ganglia, internal capsule
Septic encephalopathy	Delirium	The commonest encephalopathy in ICU

Thyroid

	Neurological features
Hypothyroidism	Slowed cognition, myopathy with raised CK, delayed ankle reflex relaxation, carpal tunnel syndrome, ataxia, myxoedema coma
Hyperthyroidism	Tremor, proximal myopathy, thyrotoxic periodic paralysis (Asian men), chorea, thyroid eye disease, seizures
Steroid-responsive encephalopathy with autoimmune thyroiditis (SREAT, Hashimoto's encephalopathy)	Encephalopathy, myoclonus, seizures, stroke-like episodes; anti-TPO antibodies; diagnosis of exclusion

Nutritional deficiencies

Vitamin B12

- Subacute combined degeneration: dorsal columns (vibration, proprioception, sensory ataxia) and lateral corticospinal tracts (spastic weakness, extensor plantars) with absent ankle reflexes from neuropathy.
- Also neuropathy, optic neuropathy, cognitive and psychiatric change, megaloblastic anaemia (may be absent).
- Causes: pernicious anaemia, gastrectomy or bariatric surgery, ileal disease, vegan diet, metformin, PPIs, **nitrous oxide** (inactivates B12).
- Diagnosis: B12 may be borderline; **raised methylmalonic acid** and homocysteine. MRI: dorsal column T2 hyperintensity ("inverted V").
- Treatment: IM hydroxocobalamin (1 mg on alternate days until no further improvement, then every 2 months, BSH/NICE); early treatment gives the best recovery. Do not give folate alone.

Copper deficiency gives an identical myelopathy: after bariatric surgery or with **zinc excess** (denture cream); anaemia and neutropenia.

Thiamine (B1)

- **Wernicke's encephalopathy:** confusion, ophthalmoplegia (nystagmus, VI palsy, gaze palsies), ataxia. The full triad is present in only ~10–20 % — treat on suspicion (Caine criteria: 2 of dietary deficiency, eye signs, cerebellar dysfunction, altered mental state or mild memory impairment).
- Causes: alcohol, malnutrition, hyperemesis gravidarum, bariatric surgery, cancer, refeeding.
- MRI: symmetric T2/FLAIR signal in the medial thalami, mammillary bodies, periaqueductal grey and tectal plate; mammillary body enhancement.
- Treatment: **IV thiamine 500 mg three times daily** for 3–5 days (EFNS), then 250 mg daily; correct magnesium.
- **Korsakoff syndrome:** anterograde and retrograde amnesia with confabulation; persistent.

Thiamine and glucose. In anyone at risk of Wernicke's, give IV thiamine before or with glucose — glucose can precipitate or worsen Wernicke's. But **never delay treatment of hypoglycaemia** to wait for thiamine.

Other deficiency	Neurological picture
Vitamin E	Spinocerebellar syndrome, neuropathy, retinopathy (fat malabsorption, <i>TTPA</i> — ataxia with vitamin E deficiency)
Niacin (pellagra)	Dermatitis, diarrhoea, dementia
Pyridoxine	Deficiency (isoniazid): neuropathy, seizures in infants; excess: sensory neuronopathy
Folate	Neuropathy, cognitive impairment, neural tube defects

Drug-induced neurological disorders

Disorder	Drugs
Parkinsonism, acute dystonia, akathisia, tardive dyskinesia	Dopamine antagonists — antipsychotics, metoclopramide, prochlorperazine; valproate (parkinsonism, tremor)
Neuroleptic malignant syndrome	Antipsychotics (or abrupt levodopa withdrawal): rigidity, hyperthermia, autonomic instability, high CK; stop drug, cooling, dantrolene, bromocriptine
Serotonin syndrome	SSRIs, SNRIs, MAOIs, tramadol, linezolid, triptans rarely: clonus (inducible, ocular), hyperreflexia, hyperthermia; cyproheptadine
PRES	Calcineurin inhibitors, chemotherapy, bevacizumab
Peripheral neuropathy	Vincristine, platinum, taxanes, bortezomib, thalidomide, metronidazole, nitrofurantoin, isoniazid, amiodarone, nitrous oxide
Myopathy	Statins, steroids, colchicine, hydroxychloroquine, zidovudine
Immune checkpoint inhibitors	Myasthenia (with myositis and myocarditis), myositis, GBS-like neuropathy, encephalitis, aseptic meningitis
CAR T-cell therapy	ICANS — encephalopathy, aphasia, seizures, cerebral oedema; steroids
Seizures	Bupropion, tramadol, carbapenems, cefepime (with renal failure), theophylline, local anaesthetics
IIH	Tetracyclines, retinoids, vitamin A, lithium, steroid withdrawal

ICU-acquired weakness

	Critical illness polyneuropathy	Critical illness myopathy
Pathology	Axonal sensorimotor neuropathy	Loss of thick (myosin) filaments; muscle inexcitability
Sensory	Reduced distally	Normal
CK	Normal	Normal or raised

	Critical illness polyneuropathy	Critical illness myopathy
NCS/EMG	Low CMAP and SNAP	Low, long-duration CMAP; normal SNAP; reduced direct muscle stimulation
Risk factors	Sepsis, multi-organ failure, hyperglycaemia	High-dose steroids with neuromuscular blockers

Often coexist (CIPNM). Present as difficulty weaning and flaccid symmetric limb weakness with facial sparing. Prevention: glycaemic control, minimise sedation and steroids/NMBAs, early mobilisation. Recovery over weeks (myopathy) to months (neuropathy).

Other systemic diseases

- **Sarcoidosis:** facial palsy (often bilateral), hypothalamic–pituitary disease, leptomeningeal and pachymeningeal enhancement, myelitis with dorsal subpial enhancement ("trident" on axial), small-fibre neuropathy.
- **SLE:** seizures, psychosis, stroke (antiphospholipid), chorea, myelitis, neuropathy.
- **Sjögren's:** sensory ganglionopathy, small-fibre neuropathy, NMOSD association.
- **Behçet's:** brainstem–diencephalic parenchymal disease, venous sinus thrombosis.
- **Coeliac disease:** gluten ataxia, neuropathy, occipital calcification with epilepsy.
- **Cardiac surgery and endocarditis:** embolic stroke, mycotic aneurysms.

Pattern recognition — Chapter 14

Sign	Description	Condition
Medial thalamic, mammillary body and periaqueductal signal	Symmetric T2/FLAIR; mammillary enhancement	Wernicke's encephalopathy
Bilateral paramedian thalamic infarcts	Single vessel	Artery of Percheron occlusion
Bilateral thalamic swelling with haemorrhage	Venous congestion	Deep cerebral venous thrombosis
Posterior subcortical vasogenic oedema	Parieto-occipital, reversible	PRES (hypertension, eclampsia, calcineurin inhibitors, chemotherapy)
Central pontine trident-shaped T2 lesion	Spare the periphery and corticospinal tracts	Osmotic demyelination
Bilateral pallidal T1 hyperintensity	—	Chronic liver disease (manganese), TPN
Inverted V in the dorsal cord	Dorsal column T2 signal	B12 or copper deficiency, nitrous oxide

Paediatric Neurology Essentials

Key tables: Febrile seizures · Infantile epileptic spasms · Hypoxic–ischaemic encephalopathy · Neurocutaneous syndromes · Spinal muscular atrophy

Febrile seizures

- The commonest seizures of childhood: 2–5 % of children aged **6 months to 5 years**, with fever $\geq 38^\circ\text{C}$ and no CNS infection or previous afebrile seizure.
- **Simple:** generalised, < 15 minutes, once in 24 hours. **Complex:** focal, ≥ 15 minutes, or recurrent within 24 hours.
- Recurrence ~30 % (higher if first seizure under 18 months, low fever at onset, short fever duration, family history).
- Later epilepsy: simple ~1–2 % (baseline ~1 %); complex 4–12 %.
- Management: treat the cause of fever, explain and reassure; rescue buccal midazolam or rectal diazepam for seizures > 5 minutes. Antipyretics do not prevent recurrence; long-term ASMs are not indicated. LP if meningitis is suspected (consider strongly under 12 months or after antibiotics). Prolonged or recurrent febrile seizures with hemiclonic features in infancy → think of Dravet syndrome (*SCN1A*).

Infantile epileptic spasms syndrome (West syndrome)

- Onset 1–24 months (peak 3–12 months).
- Clusters of brief flexor or extensor spasms, often on waking; **hypsarrhythmia** on EEG; developmental plateau or regression (West syndrome = all three).
- Causes: structural (HIE, malformations), **tuberous sclerosis**, Down syndrome, metabolic, genetic (*CDKL5*, *STXBP1*, *ARX*); a third unknown.
- Treatment is urgent — delay worsens development. First line: hormonal therapy (high-dose prednisolone or ACTH) **or vigabatrin**; vigabatrin first in tuberous sclerosis. Combined prednisolone plus vigabatrin achieved faster spasm cessation (ICISS 2017). Vigabatrin: visual field constriction, reversible MRI signal in the basal ganglia and thalami.

Hypoxic–ischaemic encephalopathy

Sarnat stage	Features	Outcome
1 Mild	Hyperalert, irritable, normal or increased tone, dilated pupils, < 24 h	Usually normal
2 Moderate	Lethargy, hypotonia, small pupils, bradycardia, seizures common	Variable — ~20–40 % abnormal
3 Severe	Stupor or coma, flaccid, absent reflexes, suppressed EEG	High mortality and disability

Therapeutic hypothermia (33.5 °C for 72 h, started within 6 h of birth) for moderate–severe HIE at ≥ 36 weeks reduces death or disability (TOBY, NICHD, CoolCap). MRI patterns: basal ganglia–thalamus (acute profound), watershed (partial prolonged), PLIC signal loss predicts poor motor outcome.

Neurocutaneous syndromes

Syndrome	Genetics	Key features
Neurofibromatosis type 1	<i>NF1</i> , chromosome 17, AD	≥ 6 café-au-lait macules, axillary/inguinal freckling, neurofibromas (plexiform), Lisch nodules, optic pathway glioma, sphenoid wing dysplasia, learning difficulties; MEK inhibitor selumetinib for plexiform neurofibromas
NF2-related schwannomatosis	<i>NF2</i> , chromosome 22, AD	Bilateral vestibular schwannomas, meningiomas, ependymomas, juvenile cataract; bevacizumab for growing schwannomas
Tuberous sclerosis complex	<i>TSC1</i> (9q) / <i>TSC2</i> (16p), AD	Hypomelanotic macules, facial angiofibromas, shagreen patch, ungual fibromas; cortical tubers, subependymal nodules, SEGA at the foramen of Monro; spasms and epilepsy; cardiac rhabdomyoma, renal angiomyolipoma, LAM; mTOR inhibitor everolimus for SEGA, angiomyolipoma, seizures
Sturge-Weber syndrome	Somatic <i>GNAQ</i> mosaicism, sporadic	Port-wine stain in V1, leptomeningeal angioma, glaucoma, seizures, hemiparesis; tram-track gyriform calcification, hemiatrophy
von Hippel-Lindau	<i>VHL</i> , chromosome 3p, AD	Cerebellar, spinal and retinal haemangioblastomas, renal cell carcinoma, pheochromocytoma, endolymphatic sac tumour
Ataxia telangiectasia	<i>ATM</i> , AR	Ataxia from early childhood, oculomotor apraxia, conjunctival telangiectasia, immunodeficiency, lymphoma, raised AFP, radiosensitivity

Spinal muscular atrophy

Autosomal recessive; homozygous deletion (or mutation) of ***SMN1*** on chromosome 5q. The number of ***SMN2*** copies modifies severity.

Type	Onset	Highest motor milestone
0	Prenatal	None; neonatal respiratory failure
1 (Werdnig-Hoffmann)	< 6 months	Never sits
2	6–18 months	Sits, never walks
3 (Kugelberg-Welander)	> 18 months	Walks (may lose it)
4	Adult	Mild proximal weakness

Proximal symmetric weakness, hypotonia, areflexia, tongue fasciculation, bell-shaped chest with paradoxical breathing; normal cognition.

Therapy	Mechanism	Route
Nusinersen	Antisense oligonucleotide modifying <i>SMN2</i> splicing	Intrathecal, maintenance every 4 months
Risdiplam	Small-molecule <i>SMN2</i> splicing modifier	Oral daily
Onasemnogene Apeparvovec	AAV9 gene replacement of <i>SMN1</i>	Single IV infusion; hepatotoxicity, thrombotic microangiopathy; best before symptoms

Key SMA trials. - **ENDEAR (2017)** – **nusinersen** in infantile-onset (type 1) SMA: 51 % motor-milestone responders vs 0 % with sham; 47 % lower risk of death or permanent ventilation. - **START (2017)** – **onasemnogene Apeparvovec**: all 15 treated infants were alive without permanent ventilation at 20 months, against 8 % in a historical cohort; 11 of 12 high-dose infants sat unaided. - **SPR1NT and NURTURE**: pre-symptomatic treatment allows most infants to reach normal milestones – the case for newborn screening.

Pattern recognition — Chapter 15

Sign	Description	Condition
Tram-track calcification	Gyriform cortical calcification with leptomeningeal enhancement and hemiatrophy	Sturge–Weber syndrome
Cortical tubers and subependymal nodules	Cortical/subcortical T2 hyperintensities; calcified ventricular nodules	Tuberous sclerosis
SEGA	Enhancing growing mass at the foramen of Monro	Tuberous sclerosis
Café-au-lait macules	≥ 6, > 5 mm before puberty, > 15 mm after	NF1
Focal areas of signal intensity (UBOs)	T2 hyperintensities in basal ganglia, cerebellum, brainstem without mass effect	NF1
Molar tooth sign	Thick, elongated superior cerebellar peduncles, deep interpeduncular fossa, vermian hypoplasia	Joubert syndrome
Lissencephaly	Smooth, agyric cortex	<i>LIS1</i> , <i>DCX</i> migration disorders

Neurogenetics

Key tables: Inheritance patterns · Repeat expansion disorders · Hereditary ataxias · CMT classification · Mitochondrial syndromes

Inheritance patterns

Pattern	Characteristics	Examples
Autosomal dominant	Vertical transmission; 50 % risk to each child; variable penetrance and expressivity	Huntington's, most SCAs, CMT1A, DM1
Autosomal recessive	Siblings affected; 25 % risk; consanguinity	Wilson's, Friedreich ataxia, SMA
X-linked	Males affected, carrier females (may be manifesting); no male-to-male transmission	Duchenne and Becker, Kennedy disease, CMTX1, adrenoleukodystrophy
Mitochondrial (mtDNA)	Maternal transmission; heteroplasmy and threshold effects	MELAS, MERRF, LHON, NARP
Repeat expansions	Anticipation (earlier, more severe onset in later generations)	HD and SCAs (paternal), DM1 (maternal congenital), fragile X (maternal)
Imprinting	Expression depends on parent of origin	Angelman (maternal <i>UBE3A</i>), Prader–Willi (paternal 15q11–13)

Repeat expansion disorders

Disorder	Gene	Repeat	Inheritance	Features
Huntington's disease	<i>HTT</i>	CAG (coding, polyglutamine)	AD	Chorea, cognitive and psychiatric decline
SCA 1, 2, 3, 6, 7, 17	Various	CAG	AD	Ataxia plus: SCA2 slow saccades and neuropathy; SCA3 (Machado–Joseph, commonest worldwide) dystonia and bulging eyes; SCA6 pure, late, episodic; SCA7 retinal degeneration
Dentatorubral–pallidoluysian atrophy	<i>ATN1</i>	CAG	AD	Myoclonic epilepsy, ataxia, chorea, dementia; Japanese ancestry
Myotonic dystrophy type 1	<i>DMPK</i>	CTG (3'UTR)	AD	Distal and facial weakness, ptosis, myotonia, cataracts, conduction block, insulin resistance, frontal balding; congenital form via the mother
Myotonic dystrophy type 2	<i>CNBP</i>	CCTG (intron)	AD	Proximal weakness, myalgia, milder; no congenital form
Fragile X syndrome	<i>FMR1</i>	CGG > 200 (full mutation)	X-linked	Intellectual disability, autism, macro-orchidism, long face
FXTAS	<i>FMR1</i>	CGG 55–200 (premutation)	X-linked	Older men: tremor, ataxia, cognitive decline; MCP sign on MRI; premature ovarian insufficiency in women
Friedreich ataxia	<i>FXN</i>	GAA (intron)	AR	Commonest inherited ataxia; onset < 25; ataxia, areflexia, extensor plantars, dorsal column loss, cardiomyopathy, diabetes, pes cavus, scoliosis; omaveloxolone
Kennedy disease (SBMA)	<i>AR</i>	CAG	X-linked	Bulbar and limb LMN weakness, gynaecomastia
C9orf72 ALS-FTD	<i>C9orf72</i>	GGGGCC (intron)	AD	ALS, FTD, or both; psychiatric presentations

Disorder	Gene	Repeat	Inheritance	Features
CANVAS	<i>RFC1</i>	AAGGG (biallelic)	AR	Cerebellar ataxia, neuropathy (sensory neuronopathy), vestibular areflexia; chronic cough
SCA27B	<i>FGF14</i>	GAA	AD	Late-onset, episodic, downbeat nystagmus; responds to 4-aminopyridine

Hereditary ataxias — beyond the repeats

Disorder	Inheritance	Clues
Ataxia telangiectasia	AR (<i>ATM</i>)	Childhood onset, oculomotor apraxia, telangiectasia, infections, cancer, raised AFP
Ataxia with vitamin E deficiency	AR (<i>TTPA</i>)	Friedreich-like; low vitamin E; treatable
Ataxia with oculomotor apraxia 1 and 2	AR	Low albumin (AOA1), raised AFP (AOA2)
Episodic ataxia type 1	AD (<i>KCNA1</i>)	Seconds–minutes, myokymia; carbamazepine, acetazolamide
Episodic ataxia type 2	AD (<i>CACNA1A</i>)	Hours, interictal downbeat nystagmus; acetazolamide, 4-aminopyridine
Cerebrotendinous xanthomatosis	AR (<i>CYP27A1</i>)	Tendon xanthomas, cataracts, diarrhoea, ataxia; chenodeoxycholic acid

Charcot–Marie–Tooth disease

Type	Inheritance and gene	Nerve conduction	Notes
CMT1 (demyelinating)	AD; CMT1A = <i>PMP22</i> duplication (commonest CMT overall), CMT1B <i>MPZ</i>	Uniform slowing, upper-limb motor CV < 38 m/s	Thickened nerves
CMT2 (axonal)	AD; <i>MFN2</i> commonest	CV normal or mildly slowed (> 38 m/s), low amplitudes	
Intermediate	AD or X-linked	CV 25–45 m/s	
CMTX1	X-linked; <i>GJB1</i> (connexin 32)	Intermediate, patchy	Transient CNS white-matter lesions
CMT4	AR	Demyelinating, severe, early	Consanguinity
HNPP	AD; <i>PMP22</i> deletion	Focal slowing at entrapment sites	Recurrent pressure palsies; tomacula

Common features: distal wasting (inverted champagne bottle), pes cavus, hammer toes, areflexia, mild sensory loss, slow progression.

Mitochondrial disorders

Syndrome	Features	Common variants
MELAS	Stroke-like episodes (not in vascular territories, often occipital), lactic acidosis, seizures, migraine, deafness, diabetes, short stature	m.3243A>G (<i>MT-TL1</i>); L-arginine in acute episodes
MERRF	Myoclonus, epilepsy, ataxia, ragged-red fibres, lipomas	m.8344A>G (<i>MT-TK</i>)
Kearns–Sayre syndrome	CPEO + pigmentary retinopathy + onset < 20, with heart block, ataxia or CSF protein > 1 g/L	Single large mtDNA deletion (sporadic)
CPEO	Ptois, ophthalmoplegia (little diplopia), proximal myopathy	mtDNA deletions; <i>POLG</i> , <i>TWINK</i>
LHON	Sequential painless subacute central visual loss in young men	m.11778G>A (commonest), m.14484T>C (best prognosis), m.3460G>A; idebenone

Syndrome	Features	Common variants
Leigh syndrome	Infant/childhood subacute necrotising encephalomyelopathy, regression, brainstem signs	> 100 nuclear and mtDNA genes (<i>SURF1</i> , m.8993T>G)
NARP	Neuropathy, ataxia, retinitis pigmentosa	m.8993T>G/C (<i>MT-ATP6</i>) — high heteroplasmy causes Leigh
POLG-related disorders	Alpers–Huttenlocher (refractory epilepsy, liver failure), ataxia–neuropathy, CPEO	Valproate contraindicated (fatal hepatotoxicity)

Investigation: lactate (blood and CSF), MR spectroscopy lactate doublet, muscle biopsy (ragged-red and COX-negative fibres), genetics (mtDNA from muscle or urine; nuclear panels).

Wilson's disease

AR, *ATP7B* (chromosome 13). Hepatic (children) or neuropsychiatric (young adults) presentation: tremor (wing-beating), dystonia, dysarthria, parkinsonism, psychiatric change. **Kayser–Fleischer rings** in almost all neurological cases. Low caeruloplasmin, high 24-h urinary copper, liver copper; MRI face of the giant panda. Chelation (penicillamine, trientine) and zinc; neurological worsening on starting chelation is possible.

Genetic testing — principles

- Pre- and post-test counselling, especially for predictive testing of adult-onset untreatable disease (Huntington's protocol).
- Repeat expansions are missed by standard exome and short-read panels — request repeat-specific tests (or long-read sequencing).
- Variants of uncertain significance are not actionable.
- Children are not tested predictively for adult-onset untreatable disorders.

Pattern recognition — Chapter 16

Sign	Description	Condition
Bilateral symmetric basal ganglia and brainstem T2 lesions	Lactate peak on MRS	Leigh syndrome
Stroke-like cortical lesions crossing vascular territories	Posterior predominance, evolving	MELAS
Middle cerebellar peduncle sign	Bilateral MCP T2 hyperintensity	FXTAS (also MSA)
Anterior temporal white-matter lesions	Young adult with myotonia	Myotonic dystrophy type 1 (also CADASIL)
Face of the giant panda	Midbrain T2 signal	Wilson's disease
Parieto-occipital white-matter disease with enhancing leading edge	Boy with behavioural decline and adrenal insufficiency	X-linked adrenoleukodystrophy

Ethics, Coma and Brain Death

Key tables: Core ethical principles · Glasgow Coma Scale · Brain death determination · Capacity · Disorders of consciousness

Core ethical principles

Principle	Meaning in neurology
Autonomy	Informed consent and refusal; respecting advance decisions; supported decision-making
Beneficence	Act in the patient's best interests
Non-maleficence	Avoid harm; weigh burdens of treatment
Justice	Fair access and allocation of resources

Decision-making capacity

Capacity is **decision-specific and time-specific**, and presumed unless shown otherwise. A person has capacity if they can:

1. Understand the relevant information
2. Retain it long enough to decide
3. Use or weigh it
4. Communicate a decision

Maximise capacity (time of day, aphasia-friendly communication, interpreters). An unwise decision does not by itself prove incapacity. Without capacity, decide in the patient's best interests or follow a valid advance directive, proxy or legal representative, according to national law.

Common neurological scenarios. Driving after seizures or syncope (follow national licensing rules); genetic testing and disclosure to relatives; disclosing diagnosis in dementia; withdrawal of life-sustaining treatment after severe stroke or hypoxic injury; anti-amyloid therapy discussions; assisted dying requests where legal.

Glasgow Coma Scale

Eye opening	Verbal		Motor	
Spontaneous	4	Oriented	5	Obeys commands
To sound	3	Confused	4	Localises
To pressure	2	Words	3	Normal flexion (withdrawal)
None	1	Sounds	2	Abnormal flexion (decorticate)
		None	1	Extension (decerebrate)
			None	1

Total 3–15; severe ≤ 8, moderate 9–12, mild 13–15. Record components (e.g. E2V2M4), and "NT" when not testable (intubated). The FOUR score adds brainstem reflexes and respiration and works in intubated patients.

Disorders of consciousness

State	Features
Coma	Eyes closed, no sleep–wake cycles, no awareness
Unresponsive wakefulness syndrome (vegetative state)	Sleep–wake cycles, eyes open, reflexive behaviour only, no awareness
Minimally conscious state	Inconsistent but reproducible signs of awareness — visual pursuit, command following (MCS+), localising pain
Emergence from MCS	Functional communication or object use
Locked-in syndrome	Conscious ; quadriplegia and anarthria; vertical eye movements and blinking preserved — ventral pontine lesion
Akinetic mutism	Awake, little spontaneous movement or speech — bilateral frontal or diencephalic lesions

Use the Coma Recovery Scale–Revised repeatedly; covert consciousness can be detected by functional MRI or EEG paradigms.

Brain death (death by neurological criteria)

Irreversible loss of all functions of the brain, including the brainstem. **Legal criteria and procedures follow national law and professional codes** — they differ between countries (whole-brain vs brainstem formulations).

2023 AAN/AAP/CNS/SCCM consensus practice guideline (adults and children).

Prerequisites - Known catastrophic, irreversible brain injury explaining the findings; observe for an appropriate period (≥ 24 h after hypoxic–ischaemic injury such as cardiac arrest). - Exclude confounders: core temperature ≥ 36 °C; systolic BP ≥ 100 mmHg or MAP ≥ 60 mmHg (children: age-appropriate); no sedative or paralytic effect (drug levels or 5 half-lives, more with renal/hepatic impairment or hypothermia; train-of-four with NMBAs); no severe metabolic, electrolyte or endocrine disturbance.

Examination - Coma: no response to noxious stimuli (spinal reflexes may persist). - Absent brainstem reflexes: pupils fixed (non-reactive to light), corneal, oculocephalic and oculovestibular (cold caloric), cough and gag, no facial movement to noxious stimulus.

Apnoea test - Pre-oxygenate; normalise PaCO₂ (35–45 mmHg) and pH; disconnect or CPAP with oxygen. - Positive (consistent with brain death) if there is no respiratory effort with arterial **pH < 7.30 AND PaCO₂ ≥ 60 mmHg AND a rise of ≥ 20 mmHg above baseline**. - Abort if unstable (SBP < 100, MAP < 60, sustained desaturation, arrhythmia) and use an ancillary test.

Ancillary tests — only when the examination or apnoea test cannot be completed or interpreted (not routinely): - **Blood-flow studies**: four-vessel catheter angiography, radionuclide perfusion scintigraphy (SPECT), or transcranial Doppler (adults). - **EEG is no longer an accepted ancillary test** in the 2023 US guideline (it remains in some national protocols).

One examination suffices in adults; two separate examinations in children, with an observation interval in neonates and infants.

Spinal reflexes (triple flexion, Lazarus sign, plantar responses) can persist and do not exclude brain death. Decerebrate or decorticate posturing, or seizures, do.

End-of-life care

- Goals-of-care conversations early in progressive disease (ALS, PSP, dementia, high-grade glioma).
- Advance care planning: ventilation, gastrostomy, resuscitation, place of death.

- Symptom control: opioids for breathlessness and pain, anticholinergics for secretions, benzodiazepines for distress.
- Withholding and withdrawing treatment are ethically equivalent.
- Organ donation discussions are separated from the determination of death (dead-donor rule).

Pattern recognition — Chapter 17

Sign	Description	Condition
Absent intracranial filling	No intracranial arterial flow above the skull base on angiography	Supports brain death
Hollow skull / empty light bulb	Absent cerebral perfusion on scintigraphy	Supports brain death
Reversal sign	Diffuse cerebral hypodensity with relatively dense cerebellum and thalami	Severe hypoxic–ischaemic injury
Pseudo-subarachnoid haemorrhage	Apparent hyperdensity of the basal cisterns from diffuse oedema	Global cerebral oedema
Ventral pontine infarct	Basilar occlusion	Locked-in syndrome

Quick Reference and Emergency Protocols

Key tables: Status epilepticus · Acute stroke · Meningitis · Raised ICP · Antiseizure dosing · Normal values · Landmark trials

Status epilepticus

Phase	Time	Intervention
Stabilisation	0–5 min	ABC, oxygen, monitoring, IV access, glucose (treat < 4 mmol/L); thiamine 100–500 mg IV if at risk
First line	5–20 min	Lorazepam 0.1 mg/kg IV (max 4 mg, repeat once) or diazepam 10 mg IV; midazolam 10 mg IM/buccal/IN if no IV access
Second line	20–40 min	Levetiracetam 60 mg/kg (max 4500 mg), fosphenytoin 20 mg PE/kg, or valproate 40 mg/kg (max 3000 mg) — equivalent (ESETT); phenobarbital 15–20 mg/kg as alternative
Refractory	40–60 min	Intubate, continuous EEG; midazolam, propofol or thiopental infusion titrated to seizure or burst suppression
Super-refractory	> 24 h of anaesthesia	Ketamine, ketogenic diet, immunotherapy (NORSE/FIRES), pyridoxine in children, neurosurgery for a focal lesion

Acute ischaemic stroke

Step	Target
Door-to-imaging	≤ 20–25 min (CT/CTA ± perfusion, or MRI)
Thrombolysis	Alteplase 0.9 mg/kg (10 % bolus, rest over 1 h, max 90 mg) or tenecteplase 0.25 mg/kg bolus (max 25 mg) within 4.5 h; door-to-needle ≤ 60 min (ideal ≤ 30)
BP	< 185/110 before and < 180/105 for 24 h after lysis; without reperfusion treat only if > 220/120
Thrombectomy	LVO up to 24 h with imaging selection (Chapter 2)
Antiplatelet	Aspirin within 24–48 h (24 h after lysis, after repeat imaging)
Glucose	7.8–10 mmol/L (140–180 mg/dL); avoid hypoglycaemia
Malignant MCA infarction	Decompressive hemicraniectomy within 48 h, age ≤ 60 (DECIMAL, DESTINY, HAMLET; DESTINY II for > 60 — survival with more disability)

Bacterial meningitis

Group	Empirical treatment
< 1 month	Ampicillin + cefotaxime (or gentamicin)
1 month – 50 years	Ceftriaxone 2 g every 12 h (or cefotaxime); add vancomycin or rifampicin where penicillin-resistant pneumococci are common
> 50 years, immunosuppressed, alcohol, pregnancy	Add amoxicillin/ampicillin 2 g every 4 h (<i>Listeria</i>)
Post-neurosurgery, shunt, penetrating trauma	Vancomycin + cefepime, ceftazidime or meropenem
Encephalitis possible	Add aciclovir 10 mg/kg IV every 8 h
Adjunct	Dexamethasone 10 mg (0.15 mg/kg) every 6 h for 4 days, with or before the first antibiotic dose

Raised intracranial pressure

Head up 30°, neck neutral, avoid jugular compression; normothermia, normoglycaemia, normonatraemia; adequate sedation and analgesia; PaCO₂ 35–40 mmHg (brief hyperventilation only as a bridge to definitive treatment); osmotherapy – mannitol 0.25–1 g/kg or hypertonic saline (e.g. 3 % or 23.4 %); CSF drainage (EVD); treat the cause (evacuation, decompression). Targets in TBI: ICP < 22 mmHg, CPP 60–70 mmHg (BTF 2016). Steroids only for tumour-related vasogenic oedema – not for stroke, ICH or TBI (CRASH).

Other emergencies at a glance

Emergency	Key action
Myasthenic crisis	FVC and bulbar monitoring, airway, IVIG or PLEX, stop provoking drugs
GBS	20/30/40 rule; IVIG or PLEX; autonomic monitoring
Spinal cord compression	Dexamethasone for malignant compression, urgent MRI whole spine, surgery or radiotherapy
Cauda equina syndrome	Emergency MRI, surgical decompression
Giant cell arteritis with visual symptoms	IV methylprednisolone immediately
Pituitary apoplexy	Hydrocortisone 100 mg IV, then neurosurgical assessment
Cerebral venous sinus thrombosis	Anticoagulate, even with haemorrhagic infarction; DOAC acceptable after acute phase (ACTION-CVT, RE-SPECT CVT)
Wernicke's encephalopathy	IV thiamine 500 mg three times daily
Neuroleptic malignant syndrome	Stop the drug, cooling, fluids, dantrolene, bromocriptine
Serotonin syndrome	Stop serotonergic drugs, benzodiazepines, cyproheptadine

Antiseizure medication dosing (adults)

Drug	Start	Maintenance	Notes
Levetiracetam	250–500 mg twice daily	1000–3000 mg/day	Reduce in renal impairment; mood effects
Lamotrigine	25 mg daily (12.5 mg or 25 mg alternate days with valproate)	100–400 mg/day	Slow titration (rash); oestrogen lowers levels
Valproate	250 mg two to three times daily	1000–2500 mg/day	LFTs, platelets, ammonia; pregnancy prevention programme
Carbamazepine	100–200 mg twice daily	600–1200 mg/day	Autoinduction; hyponatraemia; HLA-B*15:02
Oxcarbazepine	300 mg twice daily	600–2400 mg/day	Hyponatraemia (more than carbamazepine)
Phenytoin	Load 15–20 mg/kg; 300 mg/day	Guided by levels (40–80 µmol/L)	Non-linear kinetics
Lacosamide	50 mg twice daily	200–400 mg/day	PR prolongation
Topiramate	25 mg daily	100–400 mg/day	Cognitive slowing, stones, weight loss
Brivaracetam	50 mg twice daily	50–200 mg/day	Fewer behavioural effects than levetiracetam
Cenobamate	12.5 mg daily	200–400 mg/day	Slow titration (DRESS); shortens QT

Normal values

CSF (adult, lumbar)	Value
Opening pressure (lateral decubitus)	10–20 cmH ₂ O (up to 25 in obesity)
Appearance	Clear, colourless
White cells	≤ 5 /μL, lymphocytes
Red cells	None
Glucose	2.8–4.2 mmol/L (50–75 mg/dL); CSF:serum ratio ≥ 0.6
Protein	0.15–0.45 g/L (15–45 mg/dL); higher with age
Lactate	1.0–2.0 mmol/L (> 3.5 suggests bacterial meningitis)

Nerve conduction (approx. adult)	Normal
Upper-limb motor conduction velocity	> 50 m/s
Lower-limb motor conduction velocity	> 40 m/s
Median distal motor latency	< 4.2 ms
F-wave latency (median / tibial)	< 31 ms / < 56 ms

Landmark trials

Trial	Finding	Impact
NASCET (1991; 1998)	Endarterectomy benefits symptomatic 70–99 % carotid stenosis; smaller benefit at 50–69 %	Urgent CEA within 2 weeks
NINDS rt-PA (1995)	Alteplase within 3 h improves outcome	First licensed stroke treatment
ECASS III (2008)	Alteplase effective at 3–4.5 h	Extended window
RE-LY (2009)	Dabigatran 150 mg superior and 110 mg non-inferior to warfarin for stroke/systemic embolism in AF, with less intracranial haemorrhage	First DOAC in AF
MR CLEAN (2015) and HERMES	Thrombectomy for anterior LVO within 6 h; NNT ~2.6 for reduced disability	Thrombectomy standard of care
DAWN, DEFUSE-3 (2018)	Thrombectomy to 24 h with mismatch	Tissue window
SELECT2, ANGEL-ASPECT (2023)	Benefit with large ischaemic core	Wider eligibility
CHANCE (2013), POINT (2018)	Short DAPT after minor stroke/TIA	21-day aspirin + clopidogrel
ISAT (2002)	Coiling vs clipping — better 1-year outcome with coiling	Endovascular first where feasible
Stupp (2005)	RT + temozolomide improves GBM survival	Standard of care
SANAD II (2021)	Lamotrigine for focal, valproate for generalised epilepsy	First-line ASM choice
ESETT (2019)	Levetiracetam, fosphenytoin and valproate equivalent in benzodiazepine-refractory SE	Second-line choice
MGTX (2016)	Thymectomy benefits non-thymomatous AChR+ MG	Thymectomy at 18–65
ORATORIO (2017)	Ocrelizumab slows PPMS progression	First PPMS DMT
Clarity AD (2023), TRAILBLAZER-ALZ 2 (2023)	Anti-amyloid antibodies slow early AD by ~27–35 %	Disease-modifying AD therapy
ENDEAR (2017), START (2017)	Nusinersen and onasemnogene transform SMA type 1	Newborn screening

"Success is the sum of small efforts, repeated day in and day out." — Robert Collier