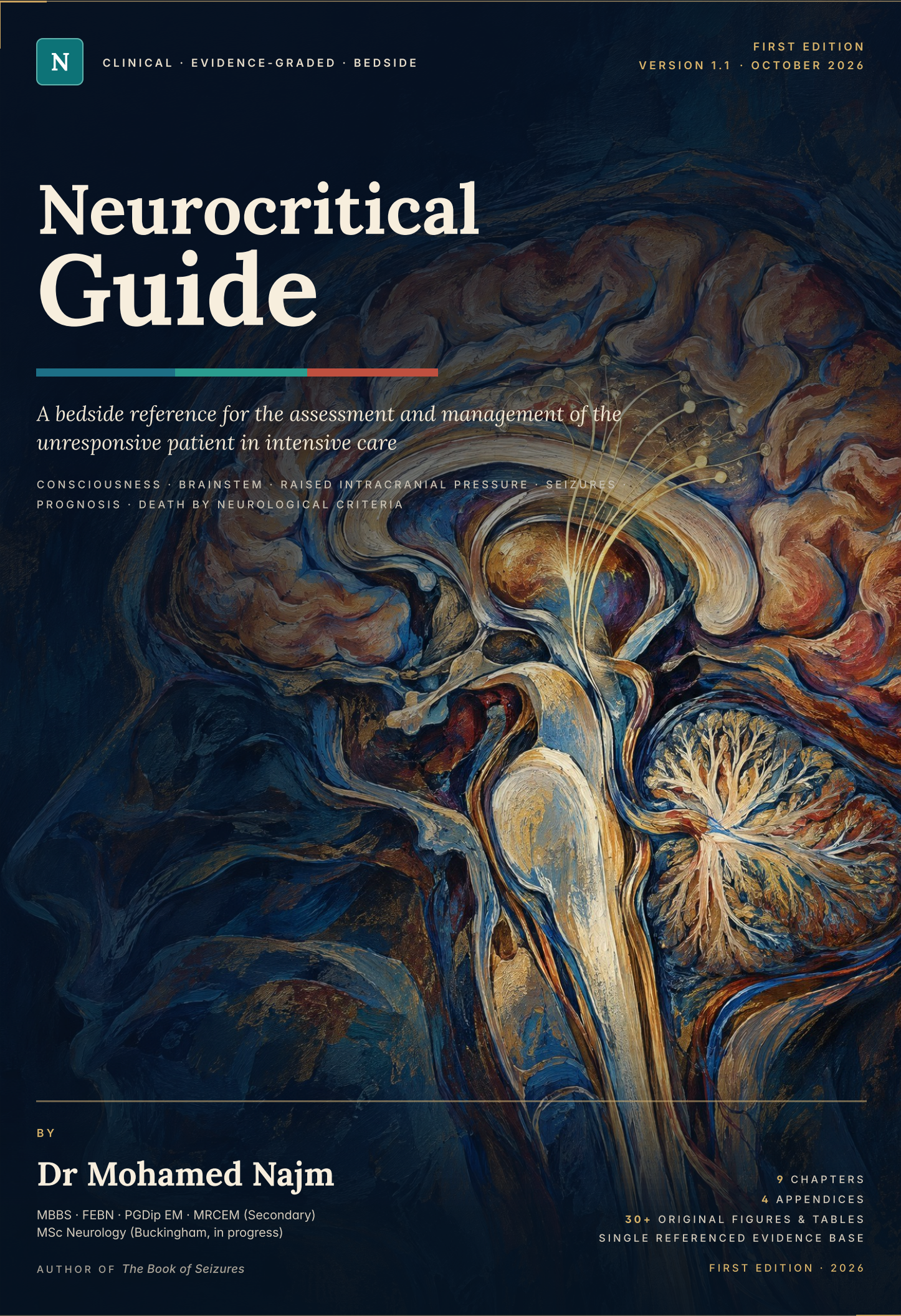




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CLINICAL · EVIDENCE-GRADED · BEDSIDE

FIRST EDITION
VERSION 1.1 · OCTOBER 2026

Neurocritical Guide

*A bedside reference for the assessment and management of the
unresponsive patient in intensive care*

CONSCIOUSNESS · BRAINSTEM · RAISED INTRACRANIAL PRESSURE · SEIZURES ·
PROGNOSIS · DEATH BY NEUROLOGICAL CRITERIA

BY

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MBBS · FEBN · PGDip EM · MRCEM (Secondary)
MSc Neurology (Buckingham, in progress)

AUTHOR OF *The Book of Seizures*

9 CHAPTERS
4 APPENDICES

30+ ORIGINAL FIGURES & TABLES
SINGLE REFERENCED EVIDENCE BASE

FIRST EDITION · 2026

Neurocritical Guide

A bedside reference for the assessment and management of the unresponsive patient in intensive care

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ILLUSTRATIONS

All figures are original schematic vector drawings created for this book. They are teaching diagrams, not anatomical atlases, and are not derived from any cited source unless a figure caption states otherwise. The cover paintings are decorative and are not anatomical illustrations.

ALSO BY THE AUTHOR

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MEDICAL DISCLAIMER

This guide is written for physicians and nurses trained in intensive care. It is not a protocol and does not replace imaging, electrophysiology, specialist consultation, institutional policy or national law. Doses are starting points for a typical adult with normal renal and hepatic function; confirm every dose against the patient's weight, organ function, drug interactions and your local formulary before administration.

Guidelines change. Each recommendation names the guideline edition it rests on; check that the edition is still current at your institution before teaching or publishing from it. The determination of death by neurological criteria must follow the national and institutional criteria in force where you practise.

EVIDENCE CURRENCY

Literature and guideline editions were reviewed to October 2026.

CONFLICTS OF INTEREST

The author declares no financial conflicts of interest and received no funding or industry support for this work.

FEEDBACK AND ERRATA

Errors and suggestions are welcome and will be corrected in the next version, with acknowledgement.

Write to contact@thetract.org.

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P Preface

This guide is built around one question: when a patient in intensive care will not wake up, what is broken, where is it, and what must be done in the next five minutes? Every page serves that question.

This is a reference book written in a bedside voice. It follows the order in which these problems present — the physiology of consciousness, the examination, localisation, pressure, the conditions that hide the examination, seizures and prognosis — and adds what a working neurointensivist needs on the same shelf: a disease-specific chapter (traumatic brain injury, aneurysmal subarachnoid haemorrhage, intracerebral haemorrhage, acute ischaemic stroke, central nervous system infection, neuromuscular respiratory failure and sodium disorders), a full chapter on death by neurological criteria, a documentation template, a drug reference and a self-assessment section.

Who it is for. Intensivists, neurologists, emergency physicians, anaesthetists, trainees and critical care nurses who look after unresponsive adults, in a neuro-ICU or a general ICU. Where invasive monitoring or continuous EEG is unavailable, the text says what to do instead.

Every threshold, dose and score is tied to a numbered reference. Where a statement rests on classical clinical neuroanatomy rather than a trial, the text says so. Where guidelines disagree, the disagreement is shown rather than hidden.

SCOPE AND LIMITS

The book covers adults. Thresholds and doses are tied to the population of the guideline or trial they come from — most ICP targets, for example, come from severe traumatic brain injury — and the text says so where it matters. It is a companion to local protocols, not a replacement for them.

HOW TO USE THIS BOOK

- **At the bedside:** start from the Emergency index on p. 6, or from the red boxes.
- **To learn:** read a chapter end to end; each opens with learning objectives and closes on a teaching point.
- **To document:** use the coma examination template in Appendix A.
- **To test yourself:** Appendix D has fourteen single-best-answer questions with explanations.
- **To check a source:** every superscript number leads to one numbered reference list.

About the author

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Also by the author

The Book of Seizures — Definitive Edition (2026)

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Its chapters on antiseizure drugs complement Chapter 7 of this guide.

A Abbreviations

ABCDEF ICU liberation bundle

ACNS American Clinical Neurophysiology Society

AES American Epilepsy Society

AIS acute ischaemic stroke

ARAS ascending reticular activating system

ASM antiseizure medication

BIPDs bilateral independent periodic discharges

BTF Brain Trauma Foundation

CAM-ICU Confusion Assessment Method for the ICU

cEEG continuous EEG

CMD cognitive motor dissociation

CN cranial nerve

CPP cerebral perfusion pressure

CPPopt optimal CPP

CRS-R Coma Recovery Scale–Revised

CSF cerebrospinal fluid

CSW cerebral salt wasting

CTA CT angiography

DCI delayed cerebral ischaemia

DNC death by neurological criteria

DoC disorder(s) of consciousness

DOAC direct oral anticoagulant

ED epileptiform discharge

EEG electroencephalography

EVD external ventricular drain

EVT endovascular thrombectomy

FOUR Full Outline of UnResponsiveness

GBS Guillain–Barré syndrome

GCS Glasgow Coma Scale

GCS-M GCS motor score

GCS-P GCS–Pupils score

GPDs generalised periodic discharges

GRDA generalised rhythmic delta activity

HSV herpes simplex virus

HTS hypertonic saline

ICH intracerebral haemorrhage

ICP intracranial pressure

IIC ictal–interictal continuum

INR international normalised ratio

IVIg intravenous immunoglobulin

LPDs lateralised periodic discharges

LRDA lateralised rhythmic delta activity

MAP mean arterial pressure

MCS minimally conscious state

MEP maximal expiratory pressure

MG myasthenia gravis

MLF medial longitudinal fasciculus

MRC Medical Research Council

NCS Neurocritical Care Society

NCSE non-convulsive status epilepticus

NIF negative inspiratory force

NPI Neurological Pupil index

NSE neuron-specific enolase

ONSD optic nerve sheath diameter

PbtO₂ brain tissue oxygen tension

PCC prothrombin complex concentrate

PE phenytoin equivalents

PLEX plasma exchange

PRIS propofol infusion syndrome

PRx pressure reactivity index

RASS Richmond Agitation–Sedation Scale

ROSC return of spontaneous circulation

SAH subarachnoid haemorrhage

SE status epilepticus

SIADH syndrome of inappropriate antidiuretic hormone

SIBICC Seattle International Brain Injury Consensus Conference

SIRPIDs stimulus-induced rhythmic, periodic or ictal discharges

SSEP somatosensory evoked potentials

TBI traumatic brain injury

TCD transcranial Doppler

TTM temperature control / targeted temperature management

UWS unresponsive wakefulness syndrome

VC vital capacity

WFNS World Federation of Neurosurgical Societies

CONVENTIONS USED IN THIS BOOK

! TIME-CRITICAL

Act now. If you read nothing else on a page, read the red box.

! CAUTION / PITFALL

Where examiners, devices or drugs mislead.

★ TEACHING POINT

The principle to carry to the next patient.

E EVIDENCE

The trial or guideline behind a practice, with its population.

Evidence badges after a statement show what it rests on: **GUIDELINE** a named society guideline; **RCT** randomised evidence; **OBS** observational cohorts; **CONSENSUS** expert consensus; **CLASSICAL** classical neuroanatomy or physiology.

REFERENCE VALUES USED IN THE TEXT

Variable	Typical adult range	Variable	Typical adult range
ICP (supine)	5–15 mmHg	Serum sodium	135–145 mmol/L
CPP	60–70 mmHg target in severe TBI	Serum osmolality	275–295 mOsm/kg
PaCO ₂	35–45 mmHg (4.7–6.0 kPa)	Glucose	Avoid < 80 and > 180 mg/dL

UNITS

Pressures in mmHg; sodium in mmol/L; osmolality in mOsm/kg; doses for adults by actual body weight unless stated. "Bilateral" in a reflex criterion means both sides tested and both absent. Times after cardiac arrest are counted from return of spontaneous circulation (ROSC). GCS terminology follows the 2014 revision.

! Emergency index — the question you arrive with

Find the bedside problem, go to the page. Red rows are minutes-matter emergencies.

At the bedside you are asking...	First action	Go to
There is a new big pupil	Call neurosurgery and senior; start the rescue drill while the scanner is arranged	p. 35
Seizing for more than 5 minutes	Benzodiazepine at full dose now	p. 51
ICP above 22 mmHg and rising	Fix the easy drivers, then escalate one tier	p. 34
Gag and cough have gone	Protect the airway; think medulla	p. 23
Hypertension, bradycardia, irregular breathing	Cushing response — treat the pressure, not the BP	p. 28
Fluctuating coma with brainstem signs	CTA now — basilar occlusion is treatable	p. 42
Fever, headache, falling GCS	Dexamethasone and antibiotics before imaging delays them	p. 43
Why will this patient not wake up?	Two-question framework; glucose first	p. 11
Is this structural or metabolic?	Look for asymmetry	p. 15
Which level is the lesion?	Bracket the highest intact and lowest lost reflex	p. 25
Not waking after sedation was stopped	Washout, drug accumulation, NCSE	p. 47
Could this be non-convulsive status?	Continuous EEG, not a 20-minute study	p. 49
Not waking after cardiac arrest	No prognosis before 72 h and clear confounders	p. 54
Eyes open but no command following	CRS-R; think CMD before calling it UWS	p. 13
Weakness with falling vital capacity	20/30/40 rule; intubate early	p. 44
Sodium falling after SAH or TBI	SIADH or salt wasting? Volume decides	p. 45
Is this brain death?	Prerequisites and mimics first	p. 58
Preparing for a family meeting	Known, unknown, and when you will know	p. 57

! THREE RULES THAT NEVER CHANGE

- **Glucose first.** Hypoglycaemia mimics every other cause of coma and is fixed in a minute.
- **Any new asymmetry is structural until imaging says otherwise.** A new unequal pupil buys a scan, not a repeat examination in an hour.
- **No prognosis on a sedated, cold, hypotensive or metabolically deranged patient.** Clear the confounders before the conversation.

1

CHAPTER ONE

Consciousness

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Separate arousal from awareness and name the anatomy of each.
- Classify coma, UWS, MCS, locked-in syndrome and cognitive motor dissociation.
- Work through the causes of coma with a two-question framework and a first-hour order.

1.1 Consciousness = arousal + awareness

Consciousness is not a single function. It has two separable components produced by two anatomically different systems, and every bedside test in this book is an attempt to probe one of them.

Arousal — the switch

Being awake at all: eyes open, sleep–wake cycling, responsiveness to the environment.

- **Generated by** the ascending arousal network of the upper pons and midbrain, relayed through thalamus, hypothalamus and basal forebrain.
- **Tested by** eye opening (spontaneous, to voice, to pressure) and brainstem reflexes.
- **Lost in** brainstem stroke or haemorrhage, herniation, sedation, profound metabolic suppression.

Awareness — the content

Knowing self and surroundings: following a command, tracking, purposeful behaviour.

- **Generated by** widespread thalamocortical and cortico-cortical networks of both hemispheres.
- **Tested by** command following, visual pursuit, object localisation, intelligible verbal or gestural communication.
- **Lost in** diffuse hypoxic–ischaemic injury, metabolic and septic encephalopathy, NCSE, bilateral hemispheric lesions.

The separation matters because it limits the possible faults in an unresponsive patient: either the switch is off, or the networks it powers are not working, or both. Without arousal, awareness cannot be assessed at all — so a comatose patient's cortex is untestable by bedside examination, which is why electrophysiology and imaging enter the assessment early.¹ **CLASSICAL**

The reverse is not true. A patient can be fully aroused — eyes open, sleep–wake cycles preserved — and show no behavioural evidence of awareness. That dissociation defines the unresponsive wakefulness syndrome, and the word *behavioural* is chosen deliberately: some of these patients are aware but cannot show it (p. 13).

The first question at every unresponsive bed is not "how deep?" but "which half is broken — the switch or the content?"

★ **TEACHING POINT**

- Loss of either component impairs consciousness; loss of both produces coma.
- A focal lesion that abolishes arousal must sit in the upper brainstem or bilateral diencephalon. A lesion that abolishes awareness while sparing arousal is almost always bilateral and hemispheric.

1.2 The states of impaired consciousness

Because the two components are independent, the combination of findings names the syndrome. The table uses current terminology from the 2018 AAN/ACRM/NIDILRR guideline.²

State	Arousal	Awareness	At the bedside
Coma	Absent	Absent	Eyes closed to all stimulation, no sleep–wake cycling, no purposeful response.
Unresponsive wakefulness syndrome (UWS / vegetative state)	Present	No behavioural evidence	Eyes open, sleep–wake cycles, reflexive behaviour only. No reproducible command following, pursuit or localisation.
Minimally conscious state minus (MCS–)	Present	Partial, fluctuating	Non-linguistic signs: visual pursuit, localisation to pain, object manipulation, contingent emotional responses.
MCS plus (MCS+)	Present	Partial, with language	Reproducible command following, intelligible words, or intentional yes/no communication — even if inaccurate.
Emerged from MCS (eMCS)	Present	Present	Functional communication or functional use of two objects, reliably and consistently.
Cognitive motor dissociation (CMD)	Present	Present, covert	No behavioural response at the bedside, but wilful brain activity to command on task-based fMRI or EEG.
Locked-in syndrome	Present	Fully present	Quadriplegia and anarthria; vertical eye movement and blinking preserved. Must never be mistaken for coma.
Pharmacological suppression	Suppressed	Suppressed	Sedation, anaesthesia, intoxication — reversible. Document drug, dose and time stopped.

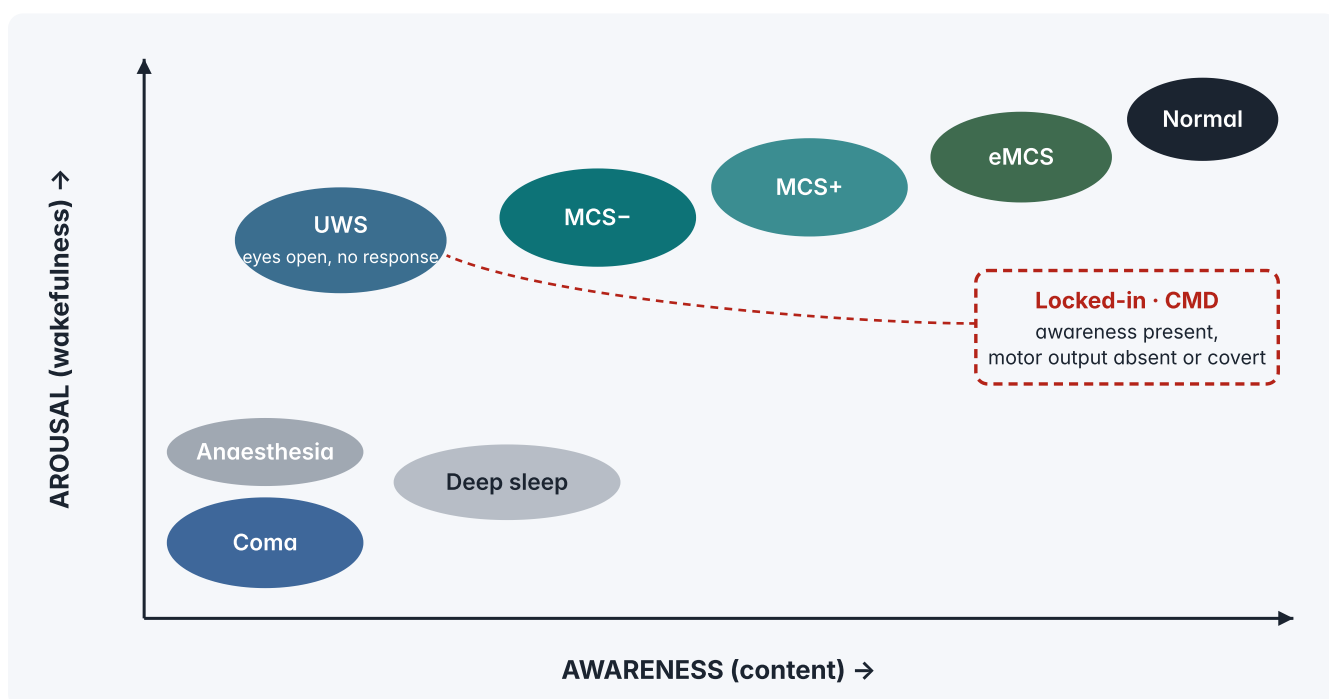


Figure 1.1 The arousal–awareness plane. Locked-in syndrome and cognitive motor dissociation sit with UWS at the bedside but belong with full awareness — the commonest and most consequential misclassification in disorders of consciousness. Original schematic.

! NEVER MISS LOCKED-IN SYNDROME

Ask every apparently unresponsive patient to **look up, look down** and **blink twice**. A ventral pontine lesion abolishes everything else. The patient hears every word said at the bedside.

1.3 The ascending arousal network — anatomy

The ascending reticular activating system (ARAS) is a network, not a tract. Its job is to raise the excitability of the forebrain; it carries no content of its own.

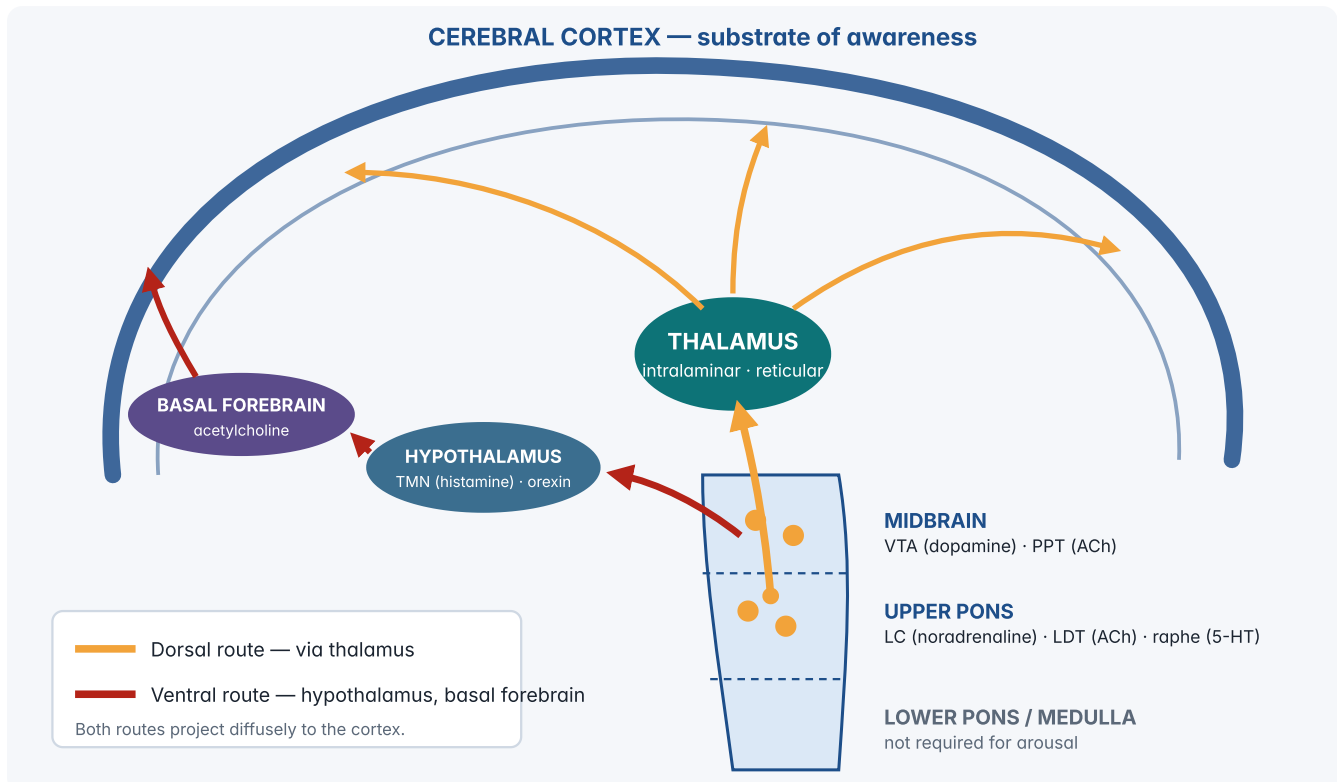


Figure 1.2 The ascending arousal network. Nuclei in the upper pons and midbrain tegmentum project dorsally to the thalamus and ventrally through hypothalamus and basal forebrain; both routes reach the cortex diffusely. LC, locus coeruleus; LDT/PPT, laterodorsal and pedunculopontine tegmental nuclei; TMN, tuberomammillary nucleus; VTA, ventral tegmental area. Original schematic after Edlow et al.³

WHY THE ANATOMY IS CLINICALLY USEFUL

The critical generator is small and lies above the mid-pons. A lesion of a few cubic centimetres in the paramedian midbrain or upper pontine tegmentum can abolish consciousness, while a large unilateral hemispheric infarct may not.^{1,3} Each point on the pathway fails differently: a pontine haemorrhage destroys the generator; uncus herniation compresses the midbrain from the side; bilateral paramedian thalamic infarction (artery of Percheron) interrupts the relay; diffuse axonal injury shears the fibres between.

! BEDSIDE COROLLARY

- A unilateral hemispheric lesion alone almost never causes coma.
- If a patient with a unilateral mass is comatose, assume the mass is now compressing the diencephalon or midbrain, and manage as herniation until imaging proves otherwise (p. 35).
- Lesions below the mid-pons do not cause coma by themselves — think locked-in syndrome.

C CASE IN PRACTICE — SMALL LESION, DEEP COMA

A 61-year-old is found unrousable with small, sluggish pupils and a vertical gaze palsy. Limbs move symmetrically to pain. The first CT is normal and the team suspects an overdose.

Resolution. MRI the next morning shows bilateral paramedian thalamic infarcts from occlusion of an artery of Percheron. A lesion of a few millilitres at the relay produced coma; symmetry and a normal early CT are not reassurance when the eyes point to the diencephalon.

1.4 The arousal network — neurochemistry

The network is a set of chemically distinct nuclei with redundant function. Every sedative used in the ICU, and most drugs that cause delirium, act somewhere on this list.

Nucleus	Transmitter	Role	ICU relevance
Locus coeruleus (pons)	Noradrenaline	Alertness, attention	Site of action of dexmedetomidine (α_2 agonist) — sedation from which the patient can be roused.
Dorsal raphe	Serotonin	Wakefulness, mood	Serotonergic toxicity alters arousal; contributes to sleep–wake cycling.
Pedunculopontine and laterodorsal tegmental	Acetylcholine	Thalamocortical activation	Anticholinergic load is a major delirium driver; cholinergic tone falls in sepsis and with age.
Ventral tegmental area, periaqueductal grey	Dopamine	Motivation, arousal	Antipsychotics blunt it; relevant to abulia and akinetic mutism after injury.
Tuberomammillary nucleus (hypothalamus)	Histamine	Wakefulness	Why first-generation H1 antihistamines sedate.
Lateral hypothalamus	Orexin (hypocretin)	Stabilises wakefulness	Loss causes narcolepsy; orexin antagonists are hypnotics.
Basal forebrain	Acetylcholine, GABA	Cortical activation	Ventral relay to the cortex, independent of the thalamus.

After Posner et al.¹ and Edlow et al.³ **CLASSICAL**

WHY SEDATION REPRODUCES BRAINSTEM FAILURE

Propofol and benzodiazepines enhance GABA_A-mediated inhibition across the arousal nuclei and the thalamocortical system; opioids suppress the pontine arousal centres and respiratory drive. The pharmacological result is the same two components switched off — reversibly.

At high doses this extends to the brainstem reflexes the examination depends on: pupils become small and sluggish, corneal and cough responses fade, and motor responses disappear. A deeply sedated examination can look identical to structural brainstem failure.

WHAT THE NETWORK DOES NOT DO

- It enables cognition; it does not produce thought or memory.
- It is redundant: no single nucleus is essential. Coma needs bilateral damage to the paramedian upper brainstem tegmentum, or to its diencephalic targets.
- Because the projection is diffuse rather than topographic, failure affects the whole forebrain at once — which is why coma is global even when its cause is small.

★ TEACHING POINT

Every drug that sedates does so by attacking the arousal half of the equation. A sedated examination is not a neurological examination. Record the drug, the dose and the time it was stopped; the washout — not the clock — decides when the examination becomes valid (p. 47).

1 ACCUMULATION IS THE USUAL CULPRIT

Midazolam and its active metabolite (α -hydroxymidazolam glucuronide) accumulate in renal failure; fentanyl accumulates in fat after prolonged infusion; morphine-6-glucuronide accumulates in renal failure. A patient who "should" have woken 24 hours after stopping an infusion may still be pharmacologically suppressed.

1.5 Why is this patient comatose?

Consciousness requires an intact arousal network and functioning bilateral hemispheres. So the bedside question has two halves, answered in sequence — and the answer decides whether you order a scan, a glucose, an EEG or a sedation hold.

1 · Are both hemispheres failing?

Bilateral, usually diffuse — the "content" fails

- Hypoglycaemia — check it before anything else.
- Hepatic, uraemic, hypercapnic or septic encephalopathy.
- Hypoxic–ischaemic injury after cardiac arrest.
- Seizures, NCSE, prolonged post-ictal state.
- Meningitis, encephalitis, PRES, diffuse SAH.
- Drug intoxication and withdrawal.

Pattern: symmetrical, no lateralising signs, brainstem reflexes preserved until very deep.

2 · Is the arousal network failing?

Brainstem or diencephalon, usually focal

- Pontine or midbrain haemorrhage or infarct.
- **Basilar artery occlusion** — time-critical, often missed.
- Bilateral paramedian thalamic infarction.
- Brainstem compression from supratentorial herniation or a posterior fossa mass.
- Diffuse axonal injury involving the brainstem.

Pattern: focal brainstem signs — pupils, gaze, corneal reflexes — in a level-by-level distribution.

THE REVERSIBLE GROUPS — EXCLUDE THESE FIRST

Drugs and metabolic disturbance suppress the system functionally rather than destroying it. They are the two commonest reasons an ICU patient does not wake, so they are excluded before any structural diagnosis is accepted and long before any prognostic statement is made.

Group	Examples	What to do
Drugs	Propofol, benzodiazepines, barbiturates, opioids, baclofen, antipsychotics, antiseizure drugs; accumulation in renal or hepatic failure; cefepime neurotoxicity in renal failure	Sedation hold if safe; drug levels where available; allow washout; naloxone or flumazenil only in selected cases
Metabolic	Glucose, sodium, calcium, magnesium, ammonia, PaCO ₂ , thyroid, cortisol, temperature, thiamine deficiency	Correct and reassess — the examination often returns entirely
Electrical	Non-convulsive seizures, NCSE, post-ictal suppression	EEG — continuous if suspicion is high (p. 49)

! DO NOT MISS

- **NCSE** — the commonest missed cause of unexplained ICU coma; it has no motor signs.
- **Basilar occlusion** — fluctuating consciousness, gaze palsy, bilateral signs. Endovascular therapy is effective up to 24 hours in selected patients (p. 42).
- **Wernicke encephalopathy** — give thiamine before glucose when malnutrition is possible.

! TWO CAUSES CAN COEXIST

A patient with a small brainstem infarct may also be uraemic and sedated. Finding one reversible cause does not end the search; reassess after each correction and ask whether the residual deficit is now explained.

1.6 The first hour — a working order

The order below protects the brain from the secondary insults — hypoxia, hypotension, hypoglycaemia — that injure it faster than any diagnosis you are about to make.

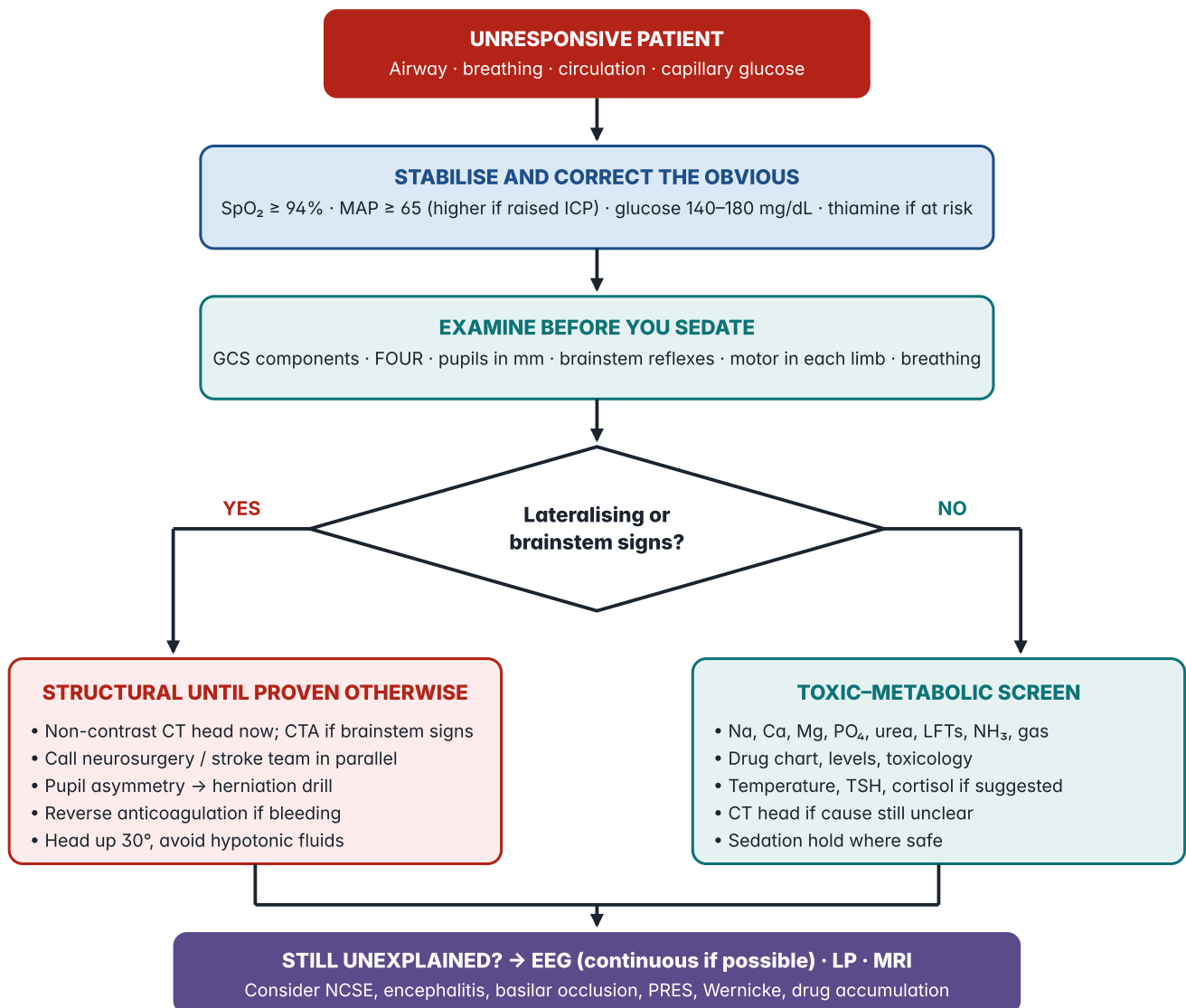


Figure 1.3 Working order for the first hour in an unresponsive adult. The two arms run in parallel when the picture is mixed. Glucose range follows common ICU practice; individual targets vary by condition. Original algorithm.

★ TEACHING POINT

Lumbar puncture follows imaging in any patient with focal signs, papilloedema, a reduced conscious level or immunosuppression — but antibiotics and dexamethasone must not wait for either when meningitis is possible (p. 43).

© CASE IN PRACTICE — THE PATIENT WHO DID NOT WAKE AFTER SURGERY

A 74-year-old with chronic kidney disease is still unresponsive 36 hours after a laparotomy, on cefepime and with a morphine PCA. Pupils are small and reactive; there is multifocal myoclonus. The CT is unchanged.

Resolution. Morphine-6-glucuronide accumulation and cefepime neurotoxicity together. EEG shows generalised periodic discharges with triphasic morphology that resolve after cefepime is switched and the opioid stopped. Two reversible causes coexisted — the first-hour order found both.

1.7 Prolonged disorders of consciousness

When a patient opens their eyes but does not follow commands, the question shifts from "why coma?" to "how much awareness is there, and how do I measure it reliably?" Bedside impressions are wrong more often than clinicians expect: misdiagnosis of MCS as UWS has been reported in roughly a third to two fifths of patients assessed without a standardised scale.² **OBS**

THE COMA RECOVERY SCALE–REVISED

The CRS-R is the recommended standardised behavioural tool.^{2,4} **AAN 2018** It has six hierarchical subscales; the highest item reached on each decides the diagnosis, not the total.

Subscale	Range	Item that signals MCS or better
Auditory	0–4	Reproducible movement to command (MCS+)
Visual	0–5	Visual pursuit or fixation (MCS–)
Motor	0–6	Localisation to noxious stimulation; object manipulation
Oromotor / verbal	0–3	Intelligible verbalisation (MCS+)
Communication	0–2	Functional, accurate communication (eMCS)
Arousal	0–3	— (attention and effort)

Total 0–23. Functional object use is a motor-subscale item that also signals emergence.

AAN 2018 RECOMMENDATIONS THAT CHANGE PRACTICE

- Use a standardised scale and **repeat it** — at least four to five assessments over a short period — because responsiveness fluctuates.
- Identify and treat confounders: sedating drugs, sleep deprivation, aphasia, visual or hearing loss, seizures, hydrocephalus.
- Replace "permanent vegetative state" with **chronic UWS**; late recovery occurs, especially after traumatic injury.
- Amantadine (100–200 mg twice daily, weeks 4–16 after traumatic injury) is recommended to hasten functional recovery. **RCT**

COGNITIVE MOTOR DISSOCIATION

In the largest multinational study to date, about one in four patients with no observable response to commands showed wilful, command-specific brain activity on task-based fMRI or EEG.⁵ **OBS** These patients are aware but cannot act. The finding was more frequent in younger patients and after traumatic injury.

! WHAT CMD MEANS AT THE BEDSIDE

- Behavioural unresponsiveness does not establish absence of awareness.
- Speak to and about every patient as if they can hear — explain procedures and treat pain.
- A "no response" CRS-R does not by itself justify a statement of permanent unawareness.

RECOVERY TIMELINES

Recovery of consciousness after the commonly cited thresholds — three months after non-traumatic and twelve months after traumatic injury — is uncommon but well documented, and some patients regain independence late.² This is why prognostic language in prolonged DoC should be graded and time-limited, not absolute.

★ TEACHING POINT

Before labelling a patient UWS: standardised scale, repeated; confounders treated; locked-in syndrome excluded; and ideally a specialist DoC opinion. Record which behaviours were sought, not just that none were seen.

E PRACTICAL CRS-R TIPS

- Assess when arousal is best — after a rest, sitting up, off sedatives; use the arousal facilitation protocol if eyes close.
- Use a mirror for visual pursuit — it is the most sensitive stimulus.
- Ask relatives which commands or objects the patient responds to; test them formally.

2

CHAPTER TWO

The bedside examination

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Run a reproducible six-step coma examination and document it so the next examiner can repeat it.
- Score GCS, GCS-P and FOUR correctly and know where each fails.
- Read the pupils, the motor response and the breathing pattern as localising signs.

2.1 The structured coma examination

The value of a neurological examination in the ICU is its repeatability, not its completeness. A short examination performed identically every few hours by every member of the team detects deterioration; a beautiful examination performed once does not.^{1,6}

1 Arousal

Eyes open spontaneously, to voice, or to pressure? Use the least stimulus that works and record it.

2 Awareness

Command following (axial and appendicular), visual fixation and pursuit, response to threat. Always test vertical eye movement and blink to command.

3 Pupils

Size in millimetres, shape, symmetry, direct and consensual reaction (p. 18).

4 Brainstem reflexes

Eye position and movements, corneal, oculocephalic or oculovestibular, cough and gag (p. 22).

5 Motor

Best response of each limb to a standard central and peripheral stimulus; tone; reflexes; abnormal movements (p. 20).

6 Breathing

Pattern, and whether the patient triggers the ventilator above the set rate (p. 21).

STIMULUS TECHNIQUE

Stimulus	Use
Voice, then loud voice	Always first. Name, then a simple command.
Fingertip pressure	Peripheral: eye opening and limb withdrawal. Pen against the side of the nail bed, building over 10 s.
Trapezius pinch	Central: localisation versus flexion. Pinch 5 cm of muscle at the neck–shoulder angle.
Supraorbital notch pressure	Central alternative. Avoid with facial fractures or orbital injury.

Stimuli as recommended for the GCS by Teasdale et al.⁷ Avoid sternal rub: it is poorly standardised and bruises.

1 STIMULUS PITFALLS

- A central stimulus is needed to distinguish localising from flexion; a peripheral one can provoke only a spinal withdrawal.
- Spinal reflexes — including triple flexion of the legs — persist after brain death.

★ TEACHING POINT

Document the time, the stimulus and the response in words. "Localises to right trapezius pinch with the left arm; right arm extends" can be repeated by the next examiner. "GCS 8" cannot.

2.2 Structural or toxic–metabolic?

Before the examination names a level, it answers a triage question: does this patient need a scanner in the next ten minutes, or a metabolic screen and a sedation hold? Asymmetry is the discriminator.¹ **CLASSICAL**

Feature	Suggests structural	Suggests toxic–metabolic
Onset	Abrupt, often with a focal deficit or headache	Gradual, fluctuating, preceded by confusion or delirium
Pupils	Asymmetric, fixed, or a new anisocoria	Symmetrical and reactive — small in opioid and pontine-like states; reaction preserved even when consciousness is deeply depressed
Brainstem reflexes	Lost in a level-by-level, rostral-to-caudal pattern	Preserved until very deep; lost globally rather than in sequence
Eye position	Conjugate gaze deviation, skew deviation, dysconjugate eyes	Roving conjugate movements; midline at rest
Motor	Hemiparesis, asymmetric posturing, unilateral Babinski	Symmetrical; tremor, multifocal myoclonus, asterixis
Breathing	Pattern localises to a level	Kussmaul (acidosis), hypoventilation (drugs), tachypnoea (sepsis, hepatic)

! ANY NEW ASYMMETRY IS STRUCTURAL UNTIL IMAGING SAYS OTHERWISE

- New anisocoria, a new focal deficit or a new gaze deviation buys an immediate CT — not a repeat examination in an hour.
- Metabolic causes can produce focal signs (hypoglycaemia, hyperosmolar states, hepatic encephalopathy), and structural lesions can look symmetrical (bilateral thalamic infarction, basilar occlusion). Asymmetry is a prompt, not a proof.

EXCEPTIONS THAT CATCH EXPERIENCED CLINICIANS

- **Hypoglycaemia** can cause hemiparesis that resolves within minutes of glucose.
- **Hepatic encephalopathy** can produce decerebrate posturing and Babinski signs while pupils stay reactive.
- **Todd paresis** after an unwitnessed seizure mimics stroke; the EEG and time resolve it.
- **Bilateral paramedian thalamic infarction** (artery of Percheron) produces symmetrical coma with vertical gaze palsy and small pupils.
- **Basilar occlusion** can be symmetrical early; look for skew, ocular bobbing and bilateral extensor plantars.
- **Diffuse SAH** may present as coma without focal signs.

WRITING IT DOWN

A trend across two examinations is worth more than any single detailed one. Use the same words, the same stimulus and the same order every time, and record the time of each examination and the sedation running at that moment. The documentation template in Appendix A (p. 62) is built for this.

★ TEACHING POINT

Pupils that stay reactive in a deeply comatose patient point strongly towards a toxic–metabolic cause. The light reflex is one of the last brainstem functions lost to metabolic suppression — except in hypothermia, anticholinergic or high-dose barbiturate toxicity, and deep anaesthesia.

2.3 The Glasgow Coma Scale and GCS-P

The GCS remains the common language of acute neurology and the input to most prognostic models. It must be scored the same way by everyone: best response, each component separately, with the 2014 terminology.^{7,8} **STANDARD**

	Eye opening (E)	Verbal response (V)	Motor response (M)
6	—	—	Obeys commands
5	—	Orientated	Localising
4	Spontaneous	Confused	Normal flexion (withdrawal)
3	To sound	Words	Abnormal flexion
2	To pressure	Sounds	Extension
1	None	None	None
NT	Not testable (e.g. swollen shut)	Not testable (e.g. intubated)	Not testable (e.g. paralysed)

GCS-PUPILS (GCS-P)

GCS-P = GCS total – Pupil Reactivity Score (PRS), where PRS is the number of pupils unreactive to light (0, 1 or 2).⁹ The range becomes 1–15, extending discrimination at the severe end where a GCS of 3 groups very different patients together. In the derivation cohorts, mortality and unfavourable outcome rose steeply across GCS-P 1–3. **OBS**

REPORT IT AS COMPONENTS

- E1V1M5 and E3V2M2 both total 7 and are not the same patient.
- The motor score carries most of the prognostic information — never bury it in a total.
- In the intubated patient write E2 VT M4, not "GCS 7T". A summed score that includes an artificial V1 is misleading.

WHERE THE GCS FAILS

Situation	Problem and remedy
Intubated	V untestable. Report E and M; add FOUR (p. 17).
Sedated	Scores the drug. Chart RASS beside it; reassess at the sedation trough.
Periorbital swelling	E untestable — record NT, not 1.
Aphasia	V under-scores an aware patient; test comprehension by gesture.
Hemiparesis	Score the <i>better</i> side for M, but record both.
Brainstem lesion	The GCS tests nothing of the brainstem. Add pupils and brainstem reflexes.

! THE NUMBERS THAT DEMAND ACTION

- A fall of **1 point in the motor score** or **2 or more points** in the total is deterioration: examine the pupils, call a senior and repeat imaging.
- A GCS of 8 or less is not by itself an indication to intubate; airway protection, gas exchange and the trajectory decide.

C CASE IN PRACTICE — TWO GCS 7S

Two patients are handed over as "GCS 7". Patient A is E1 V1 M5 after a subdural evacuation; patient B is E3 V2 M2 with a pontine haemorrhage.

Resolution. Patient A localises — a much better prognosis and a supratentorial problem. Patient B extends — a brainstem lesion. The total hid both facts; the components revealed them.

2.4 The FOUR score

The Full Outline of UnResponsiveness score was developed at the Mayo Clinic for the ICU. It drops the verbal component, which is untestable after intubation, and adds the two things the GCS misses — brainstem reflexes and respiration. Each component scores 0–4, for a total of 0–16.¹⁰

VALIDATED

	Eye response (E)	Motor response (M)	Brainstem reflexes (B)	Respiration (R)
4	Eyelids open or opened; tracking or blinking to command	Thumbs-up, fist or peace sign to command	Pupil and corneal reflexes present	Not intubated, regular breathing
3	Eyelids open but not tracking	Localising to pain	One pupil wide and fixed	Not intubated, Cheyne–Stokes
2	Eyelids closed; open to loud voice	Flexion response to pain	Pupil or corneal reflexes absent	Not intubated, irregular breathing
1	Eyelids closed; open to pain	Extension response to pain	Pupil and corneal reflexes absent	Breathes above ventilator rate
0	Eyelids remain closed with pain	No response, or generalised myoclonus status	Pupil, corneal and cough reflexes absent	Breathes at ventilator rate, or apnoea

WHY USE IT IN THE ICU

- Fully scorable in intubated patients.
- The B and R components detect rostro-caudal deterioration that the GCS cannot see.
- E4 requires tracking or blinking to command — so the score itself prompts the examiner to look for locked-in syndrome.
- A FOUR of 0 is the only score that prompts consideration of brain death testing; it does not establish it.

HONEST LIMITATIONS

- The GCS remains the lingua franca on rounds and in prognostic models.
- FOUR is a severity scale, not a disorders-of-consciousness instrument. Distinguishing UWS from MCS needs the CRS-R (p. 13).
- It needs team training; inter-rater agreement is good after training and poorer without it.
- Practical answer:** chart both — GCS components for communication, FOUR for brainstem detail.

E4 with tracking and blink to command, but M0 — that is locked-in syndrome, not coma.

★ TEACHING POINT

- A falling B component is the earliest numerical sign of brainstem compromise — it moves before the total does.
- In any patient with a mass lesion, score B and R at every examination and act on a change of one point.

❶ SCORING TRAPS

- Eye response: if the eyelids are closed, open them and check tracking against a finger or mirror before scoring E3 or below.
- Motor response 0 includes generalised myoclonic status — note it separately; it has its own prognostic meaning after cardiac arrest (p. 54).

2.5 The pupils

The pupillary light reflex is the most useful single sign in neurocritical care: its pathway is long, anatomically specific, and resistant to metabolic suppression. The parasympathetic fibres travel on the outside of the oculomotor nerve along the tentorial edge, which is why compression affects the pupil before eye movements.¹ **CLASSICAL**

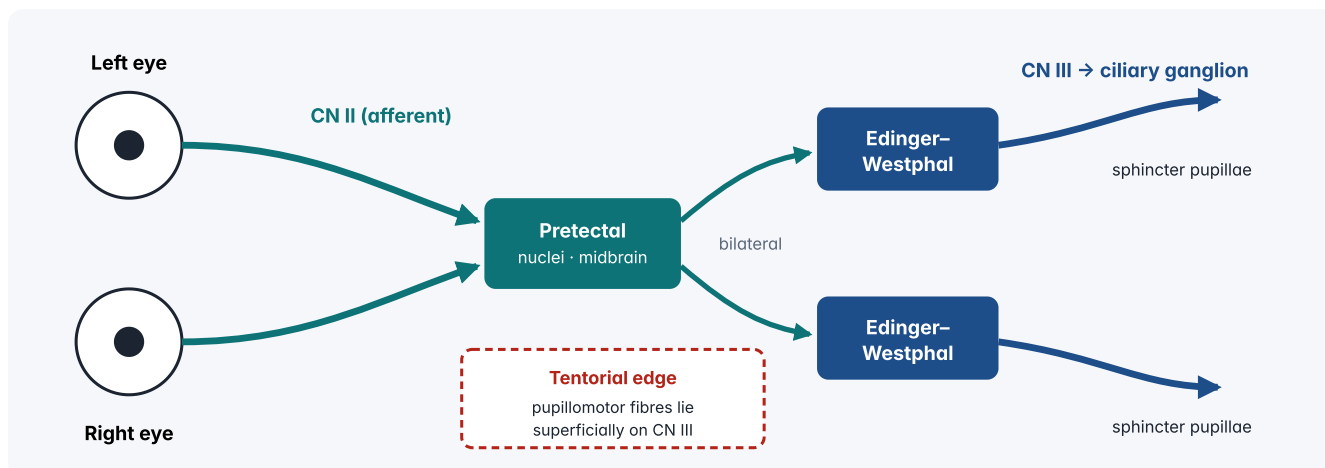


Figure 2.1 The light reflex. Light in one eye drives both Edinger–Westphal nuclei, so both pupils constrict (direct and consensual). A compressive CN III lesion abolishes constriction on its own side to light shone in either eye; an optic nerve lesion abolishes the response of both pupils to light shone in the affected eye (relative afferent defect). Original schematic.

EXAMINE IT PROPERLY

- Record size in millimetres with a pupil gauge, not adjectives.
- Bright focused light in a dimmed room; observe for several seconds. A sluggish reaction is an abnormal reaction.
- Use a magnifier or pupillometer for small pupils before calling them unreactive.
- Record shape: an oval pupil is often a transitional sign of early CN III compression.

THE SYMPATHETIC PATHWAY

Three neurons: hypothalamus → down the brainstem and cord to C8–T2 → superior cervical ganglion → along the internal carotid artery to the dilator pupillae. A lesion anywhere produces Horner syndrome: a small reactive pupil, mild ptosis and, with lesions proximal to the carotid bifurcation, facial anhidrosis. In the ICU, think lateral medullary infarction, carotid dissection, apical lung disease and central lines.

THE SWINGING LIGHT TEST

Swing a bright light briskly between the eyes, pausing about three seconds on each. If both pupils *dilate* when the light reaches one eye, that eye has a relative afferent pupillary defect (optic nerve or extensive retinal disease). The test needs only one working iris, so it remains valid when one pupil is pharmacologically or traumatically fixed.

DOCUMENTING THE PUPILS

Record	Example
Size (mm)	R 3 mm · L 6 mm — in a dimmed room
Reaction	R brisk · L none (direct and consensual)
Shape	L oval
NPi (if available)	R 4.2 · L 1.1
Context	Time; sedation running; any eye drops or nebulisers

2.6 Pupil patterns, pupillometry and mimics

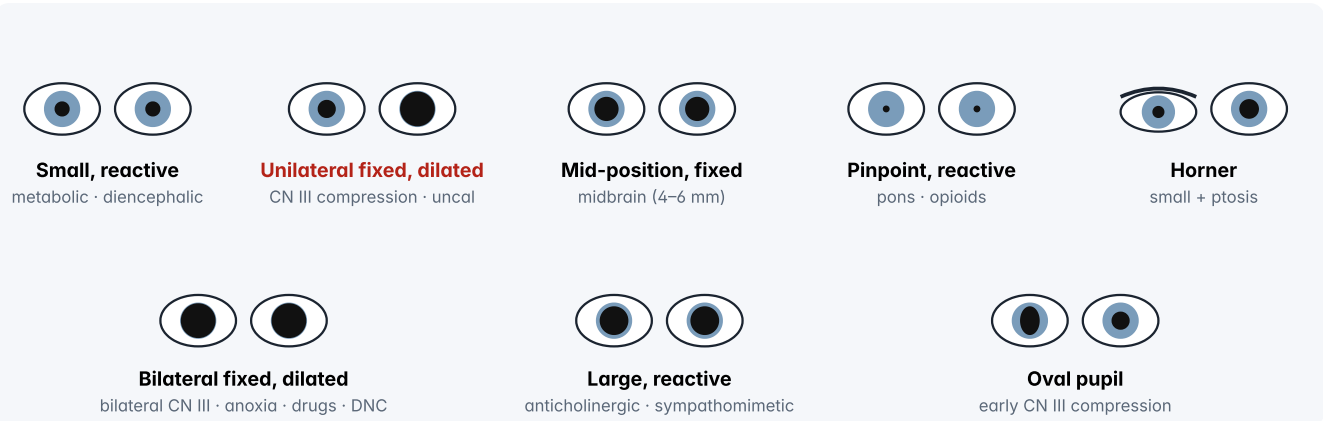


Figure 2.2 Pupil patterns in coma, viewed facing the patient. Patterns localise only in context — always pair them with the conscious level, eye movements and the drug chart. Original schematic.

QUANTITATIVE PUPILLOMETRY

An infrared pupillometer measures size, constriction velocity and latency, and combines them into the Neurological Pupil index (NPI, 0–5). By convention $\text{NPI} \geq 3$ is normal, < 3 abnormal, and 0 non-reactive; a difference of ≥ 0.7 between eyes is also abnormal.

- Removes inter-observer disagreement and detects change before the naked eye.
- In the multicentre ORANGE cohort of acute brain injury, $\text{NPI} < 3$ on any day was associated with unfavourable outcome at six months.¹¹ **OBS**
- After cardiac arrest, a very low $\text{NPI} (\leq 2)$ at ≥ 72 h has been studied as a predictor of poor outcome; use it only within a multimodal assessment.
- Treat a **downward trend** as a warning even while the standard examination looks unchanged.

BEFORE YOU CALL IT HERNIATION

Mimic	Clue
Nebulised ipratropium	Unilateral large pupil after a nebuliser; no response to 1% pilocarpine
Mydriatic drops, scopolamine patch	Drug history; other neurology unchanged
Ocular trauma, surgery, prosthesis	Irregular pupil, history, examination of the globe
Physiological anisocoria	< 1 mm, both reactive, old photographs
Adie pupil	Slow tonic constriction to near effort

! EXCLUDE IN PARALLEL, NOT FIRST

None of these mimics should delay a scan if the conscious level has also fallen. A new unilateral fixed dilated pupil is an emergency — start the rescue drill on **p. 35** while imaging is arranged.

C CASE IN PRACTICE — THE NEBULISER PUPIL

A ventilated patient with COPD and a small frontal contusion develops a 7 mm unreactive left pupil an hour after an ipratropium nebuliser. GCS components and FOUR are unchanged, and the right pupil is 3 mm and brisk.

Resolution. CT is arranged immediately and is unchanged. One drop of 1% pilocarpine fails to constrict the left pupil, confirming pharmacological blockade; a compressed third nerve would constrict. The scan was right to go first; the pilocarpine test was right to follow.

2.7 The motor examination and posturing

In an unresponsive patient the motor examination answers two questions: is there a focal deficit, and is the response purposeful or reflexive? Posturing is not weakness — it is a stereotyped release phenomenon, and its pattern carries localising and prognostic weight.¹



Abnormal flexion (decorticate)

arms flexed, adducted, wrists flexed · legs extended
lesion above the midbrain (hemispheric, diencephalic)



Extension (decerebrate)

arms extended, adducted, internally rotated · legs extended
midbrain–upper pons; also severe metabolic coma

Figure 2.3 Posturing to a central stimulus. The traditional red-nucleus explanation of the difference is derived from animal work and is imprecise in humans; extension generally implies a lower or more severe dysfunction than flexion. Original schematic.

GRADING POWER — MRC SCALE

Grade	Response
5	Normal power
4	Movement against gravity and some resistance
3	Movement against gravity only
2	Movement with gravity eliminated
1	Flicker or trace of contraction
0	No contraction

Medical Research Council.¹² Usable only in patients who can cooperate; in coma, describe the response to stimulation instead.

READING THE RESPONSE

- **Localising:** the hand moves to the stimulus and crosses the midline, or reaches above the clavicle to a supraorbital stimulus.
- **Normal flexion:** rapid withdrawal at the elbow, variable, not stereotyped.
- **Abnormal flexion:** slow, stereotyped, with wrist flexion and thumb adduction.
- Record the **best response in each limb**; asymmetry is the finding that matters.

ALSO WORTH CHECKING

- **Tone:** flaccid early after acute injury; symmetric increase in metabolic states; paratonia in diffuse cortical dysfunction.
- **Abnormal movements:** multifocal myoclonus and asterixis point to toxic–metabolic causes; subtle rhythmic twitching of face or fingers points to seizures.

! THE TREND THAT DEMANDS ACTION

Progression from flexion to extension, or new extensor posturing with a dilating pupil, means herniation is under way — go to the drill on [p. 35](#). Kernohan's notch can produce weakness on the *same* side as the mass; the pupil is the more reliable localising sign ([p. 26](#)).

C CASE IN PRACTICE — LOCALISING OR WITHDRAWING?

To right trapezius pinch, the left hand crosses the chest to the examiner's hand. To left nail-bed pressure, the arm only bends at the elbow.

Resolution. The first is localising (M5); the second is a peripheral withdrawal. Scoring only the second under-scores the patient by a motor point.

2.8 Respiratory patterns

Respiratory control is distributed down the brainstem, so the breathing pattern localises in the same way a reflex does — with a crucial caveat: the patterns are classical observations, are altered by drugs, acidosis and heart failure, and are masked by mechanical ventilation.¹ **CLASSICAL**

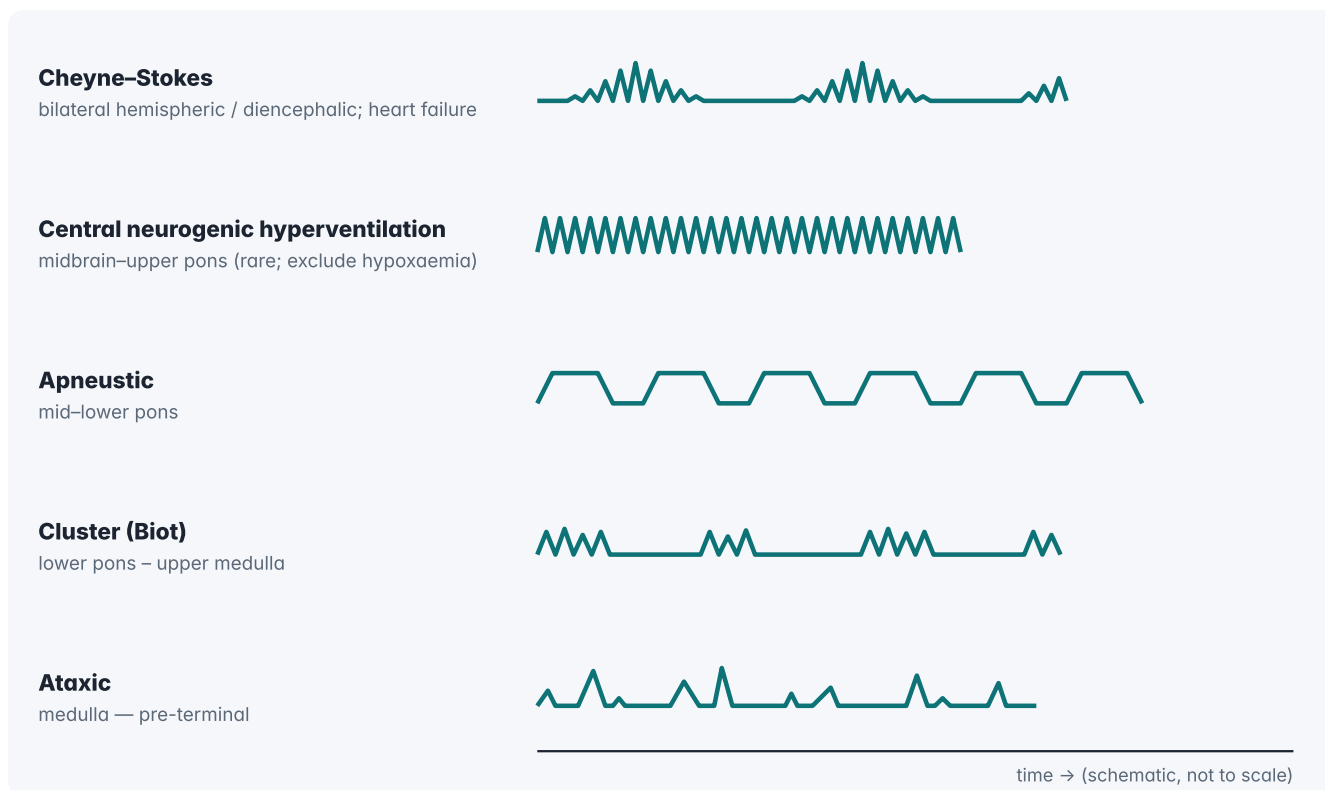


Figure 2.4 Classical breathing patterns and their approximate localisation. Original schematic after Plum and Posner.

IN THE VENTILATED PATIENT

- Breathing above the set rate tells you respiratory drive is intact — record it; it is the R1 item of the FOUR score.
- Breathing exactly at the set rate or apnoea scores R0; it does not establish apnoea, which requires a formal test (p. 60).
- Watch the flow–time waveform for spontaneous effort during any sedation hold.
- Ventilator autotriggering (cardiac oscillations, circuit leak) can mimic breathing in a patient with no drive.

DO NOT OVER-READ IT

- Opioids, sedatives, metabolic acidosis (Kussmaul), sepsis and heart failure alter the pattern independently of the brainstem.
- Cheyne–Stokes breathing is common in heart failure and in sleep in the elderly.
- Interpret the pattern alongside pupils and reflexes — never on its own.

WHAT TO RECORD

The pattern in words ("irregular in rate and depth"), whether the patient triggers the ventilator and by how much, and any apnoeic pauses with their length.

! THE MEDULLA IS FAILING

Ataxic or apneustic breathing, especially with a new loss of cough or gag, means the medullary centres are failing. Secure the airway and treat as peri-arrest (p. 23).

3

CHAPTER THREE

Brainstem and localisation

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Test each brainstem reflex correctly and name the segment it examines.
- Bracket a lesion between the highest intact and lowest lost reflex.
- Recognise each herniation syndrome before the Cushing response appears.

3.1 Brainstem reflexes and what they test

Brainstem reflexes are the only part of the examination that localises reliably in an unconscious patient. Each has an afferent nerve, an efferent nerve and a connection at a known level. If the reflex is gone, that segment — or one of its nerves — is not working.^{1,13}

Reflex	Afferent → efferent	Level	How to test	Absent means
Pupillary light	II → III	Midbrain	Bright light, each eye, direct and consensual	Midbrain dysfunction or CN III compression
Corneal	V ₁ → VII	Pons	Cotton wisp or saline drop to the cornea (not sclera); watch both lids	Pontine dysfunction (or CN V/VII lesion)
Oculocephalic (doll's eyes)	VIII → III, VI via MLF	Pons–midbrain	Brisk head rotation; eyes should move opposite to the head. Only after the cervical spine is cleared	Interrupted pontine–mesencephalic gaze pathways
Oculovestibular (cold caloric)	VIII → III, VI via MLF	Pons–midbrain	See p. 24 — the stronger stimulus	As above; definitive when equivocal
Cough	X → X (and respiratory muscles)	Medulla	Suction catheter passed to the carina	Medullary dysfunction — airway at risk
Gag	IX → X	Medulla	Stimulate posterior pharynx with a spatula or by moving the tube	Medullary dysfunction — airway at risk
Grimace to supraorbital pressure	V → VII	Pons	Supraorbital or temporomandibular pressure	Pontine dysfunction

I DRUGS SUPPRESS REFLEXES TOO

Deep sedation and neuromuscular blockade depress corneal, cough and gag responses; high-dose barbiturates, propofol and hypothermia can suppress pupils. Never interpret an absent reflex as structural without documenting the drug, the dose, the time it was stopped and — for blockade — a train-of-four.

★ TEACHING POINT

Reflexes are lost from the top down as pressure rises. The sequence of loss is the clock. Record which reflexes are present at every examination so the next examiner can see the direction of travel.

Sensitivity varies by reflex. A gag is often weak in normal elderly people and is impossible to judge with some endotracheal tubes; the cough to deep suction is the more reliable medullary test in intubated patients.

3.2 The brainstem map

The brainstem is three stacked segments, and the cranial nerve nuclei are arranged in strict order from top to bottom. Learn the order once and localisation becomes arithmetic.

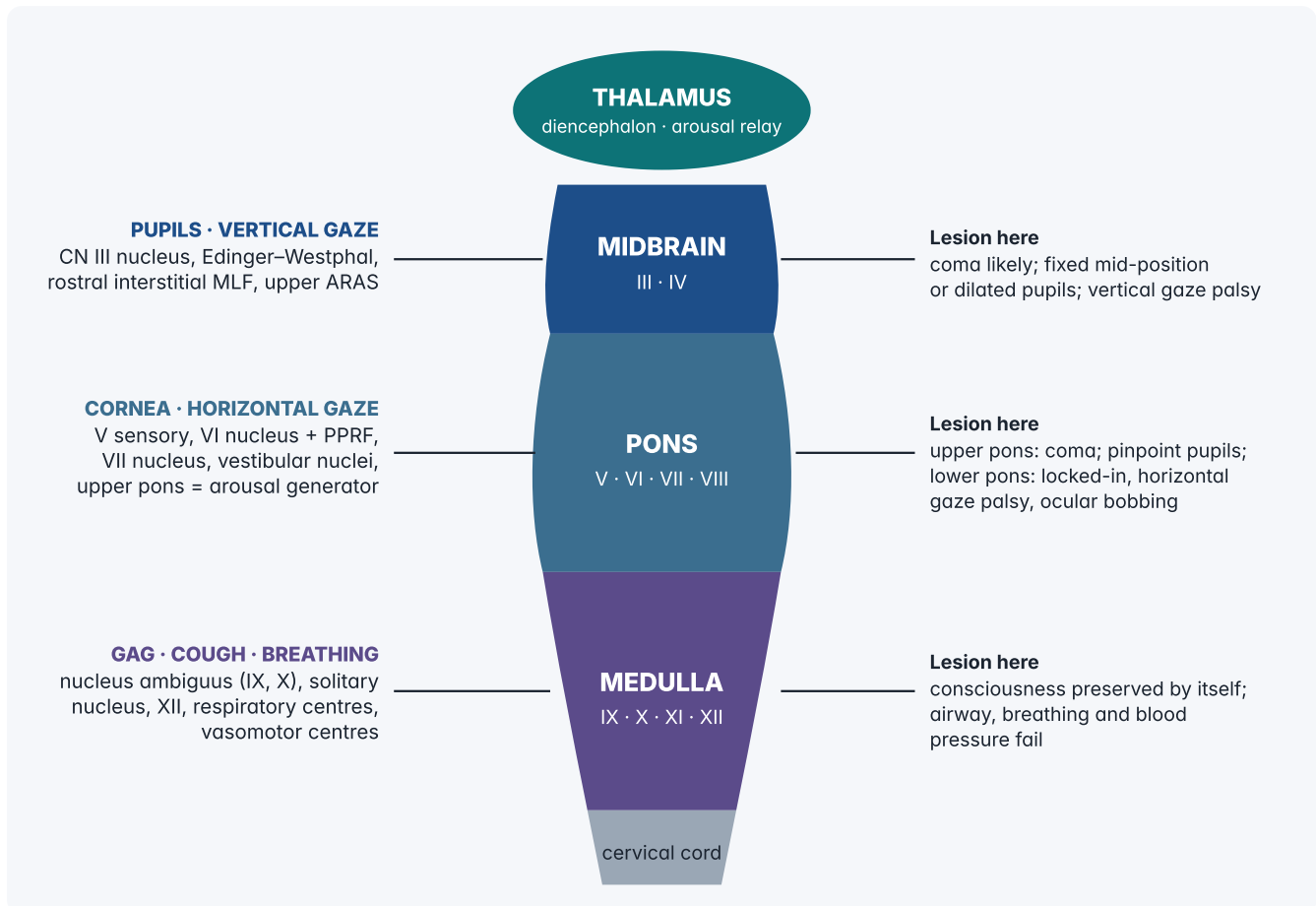


Figure 3.1 Brainstem segments, the nuclei that live in each, and what a lesion at each level does. PPRF, paramedian pontine reticular formation; MLF, medial longitudinal fasciculus. Original schematic.

! LOSE THE MEDULLA, LOSE THE AIRWAY

- Absent gag **and** cough means the patient cannot protect the airway — intubate unless goals of care say otherwise.
- Ataxic or apneustic breathing means failing medullary centres: treat as peri-arrest and escalate immediately.
- Medullary compression also destabilises blood pressure and heart rate — expect the Cushing response or sudden collapse.

HERNIATION READS TOP-DOWN

Supratentorial pressure transmits downward: diencephalon (small reactive pupils, Cheyne–Stokes) → midbrain (fixed pupils, decorticate then decerebrate posturing) → pons (loss of corneal and horizontal eye movements) → medulla (loss of cough, gag and breathing). Posterior fossa lesions can skip the sequence and compress the medulla first.

C CASE IN PRACTICE — THE MEDULLA FIRST

A 45-year-old with vertigo and vomiting has a hoarse voice, left Horner syndrome and left limb ataxia. He is alert. Overnight he develops weak cough, pooling secretions and irregular breathing.

Resolution. Left lateral medullary infarction extending medially. Consciousness is preserved because the lesion lies below the arousal generator; the airway fails because the nucleus ambiguus and respiratory centres do not. Elective intubation came first.

3.3 Eye movements, calorics and gaze

The eyes are the richest localising sign in coma. Their resting position, their spontaneous movements and their response to vestibular stimulation each say something different about the brainstem.^{1,13}

COLD CALORIC (OCULOVESTIBULAR) TECHNIQUE

1. Inspect the canal; confirm an intact tympanic membrane and remove wax or blood.
2. Head elevated 30° (brings the horizontal canal vertical).
3. Irrigate with 50 mL of ice-cold water over about a minute; observe for one minute.
4. Wait five minutes before testing the other ear.

Response in a comatose patient	Meaning
Tonic conjugate deviation toward the cold ear, no fast phase	Brainstem gaze pathways intact; cortex not generating the correcting saccade
Nystagmus with fast phase away from the cold ear	Cortex functioning — consider psychogenic unresponsiveness
Ipsilateral eye abducts, the other fails to adduct	Internuclear ophthalmoplegia — MLF lesion
Only abduction on one side, no response otherwise	CN III palsy on the side that fails to adduct
No response bilaterally	Severe pontomesencephalic dysfunction — or drug suppression (sedatives, vestibulotoxic drugs)

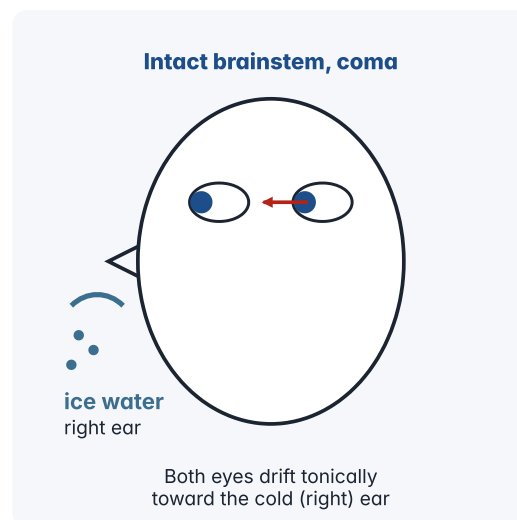


Figure 3.2 Cold calorics in coma (patient viewed from the front; patient's right on the viewer's left). Original schematic.

GAZE DEVIATION AND SPONTANEOUS EYE MOVEMENTS

Finding	Localisation and meaning
Conjugate deviation toward the lesion	Destructive hemispheric lesion (frontal eye field) — eyes look away from the hemiparesis. Overcome by calorics.
Conjugate deviation away from the lesion	Pontine lesion (eyes look <i>toward</i> the hemiparesis); seizure focus (eyes look away from the focus, often with nystagmoid jerks); thalamic haemorrhage ("wrong-way eyes").
Downward and inward deviation	Thalamic or dorsal midbrain lesion; may accompany small, poorly reactive pupils.
Skew deviation	Vertical misalignment — brainstem or cerebellar lesion.
Ocular bobbing	Fast downward jerk, slow return — classically extensive pontine lesion.
Roving eye movements	Slow, conjugate, horizontal — brainstem intact; toxic-metabolic or bihemispheric cause.
Ping-pong gaze	Horizontal deviation alternating every few seconds — bilateral hemispheric dysfunction.

3.4 Localise it — from sign to level

At the bedside you start with a finding and work backwards. Two rules do most of the work: match each lost reflex to its segment, then bracket the lesion between the highest reflex still intact and the lowest one lost.

What you find	Read it as
Unilateral fixed dilated pupil, corneals intact, falling consciousness	CN III compression at the tentorial edge — uncal herniation until proven otherwise; run the drill (p. 35)
Small reactive pupils, Cheyne–Stokes, bilateral flexion	Diencephalic stage of central herniation, or metabolic coma
Mid-position fixed pupils, extension	Midbrain — central herniation or primary midbrain lesion
Absent corneals and horizontal eye movements, pupils reactive	Pons
Absent gag and cough, pupils and corneals present	Medulla — protect the airway first
Tongue deviates on protrusion	Lower motor neuron XII lesion — tongue points <i>toward</i> the lesion. With an upper motor neuron (corticobulbar) lesion it points away.
Reflexes lost in sequence from the top down	Active rostro-caudal deterioration — escalate now

CROSSED (ALTERNATING) SYNDROMES

A cranial nerve deficit on one side with a long-tract deficit — motor or sensory — on the other is the signature of a brainstem lesion: the nerve leaves at its own level while the long tract has not yet crossed.¹ CLASSICAL

Syndrome	Findings	Level and vessel
Weber	Ipsilateral CN III palsy, contralateral hemiparesis	Ventral midbrain; PCA perforators
Benedikt / Claude	CN III palsy with contralateral tremor or ataxia (red nucleus, cerebellar outflow)	Tegmental midbrain
Millard–Gubler	Ipsilateral VI and VII palsy, contralateral hemiparesis	Ventral caudal pons
Locked-in syndrome	Quadriplegia, anarthria; vertical gaze and blink preserved	Bilateral ventral pons; basilar artery
Wallenberg (lateral medullary)	Ipsilateral facial pain–temperature loss, Horner, ataxia, dysphagia and hoarseness (IX, X); contralateral body pain–temperature loss. No hemiparesis — the crossing is sensory.	Lateral medulla; vertebral or PICA
Medial medullary (Dejerine)	Ipsilateral XII palsy, contralateral hemiparesis and loss of proprioception	Medial medulla; anterior spinal / vertebral

★ THE RULE

Pupils and vertical gaze = midbrain · corneals and horizontal gaze = pons · gag, cough and breathing = medulla. An absent gag with intact corneals localises to the medulla; the damage lies between the highest reflex still present and the lowest one lost.

3.5 False localising signs and how to resolve disagreement

Some signs point to the wrong place. Each has a mechanical explanation, and each is resolved by trusting the more reliable sign.

CN VI palsy

The abducens nerve has a long intracranial course and is stretched over the petrous apex when ICP rises or falls (including after lumbar puncture or CSF over-drainage). A unilateral or bilateral VI palsy points to **pressure**, not to the pons.

Kernohan's notch phenomenon

A large hemispheric mass shifts the brainstem so the *opposite* cerebral peduncle is pressed against the tentorial edge, producing hemiparesis on the **same** side as the mass.¹⁴ The dilated pupil usually remains on the side of the mass and is the more reliable sign.

CN III palsy from a remote cause

A posterior communicating artery aneurysm compresses CN III directly — painful, pupil-involving, without herniation. The conscious level distinguishes it from uncal herniation.

Hydrocephalus

Acute obstructive hydrocephalus causes upgaze palsy, sunset eyes and small poorly reactive pupils by dorsal midbrain compression — a midbrain-looking picture from a ventricular cause.

WHEN SIGNS DISAGREE

Conflict	Trust
Pupil on one side, hemiparesis on the same side	The pupil — consider Kernohan's notch; image now.
Gaze deviation away from the hemiparesis (toward weak side)	Pontine lesion, seizure, or thalamic haemorrhage — not a cortical stroke. EEG if no brainstem lesion.
Bilateral VI palsy, no other brainstem signs	Raised or low ICP — not a focal pontine lesion.
Unreactive pupils, preserved corneals and eye movements	Pharmacological or ocular cause, or bilateral CN III compression; check drugs and globes.
Coma with normal brainstem reflexes and normal CT	Toxic-metabolic, NCSE, encephalitis, early basilar occlusion, bilateral thalamic infarct (CT-negative early). MRI and EEG.

❶ CT CAN BE NORMAL WHEN THE BRAINSTEM IS NOT

Early ischaemia, small brainstem infarcts and posterior fossa lesions are frequently invisible on CT because of beam-hardening artefact. When the examination localises to the brainstem and CT is normal, the next test is CT angiography of the posterior circulation and then MRI with diffusion-weighted imaging.

★ TEACHING POINT

Trust the pupil and the level of consciousness over an isolated long-tract sign. When the examination and the scan disagree, believe the examination and repeat the imaging with the right modality.

3.6 Herniation syndromes

Herniation describes tissue moving from one compartment to another because pressure has become unequal. The picture depends on which structures are compressed on the way, and each pattern has a signature that appears before the patient arrests.¹

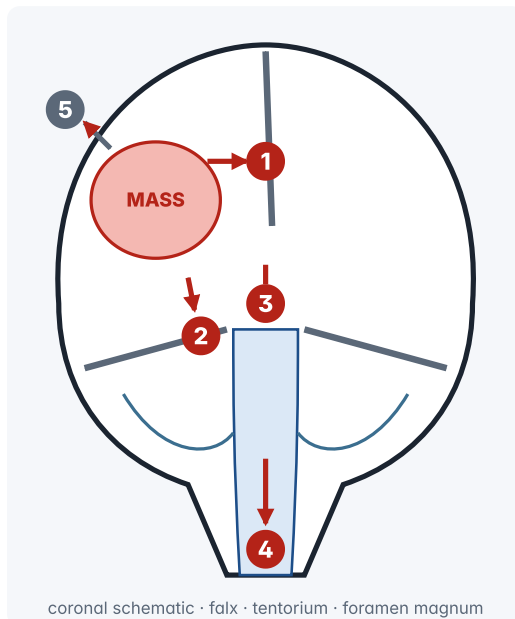


Figure 3.3 Herniation from a left hemispheric mass. 1 subfalcine; 2 uncal (lateral transtentorial); 3 central (axial) transtentorial; 4 tonsillar; 5 external (through a skull defect). Upward herniation is not shown. Original schematic.

Syndrome	Signature
1 Subfalcine	Cingulate gyrus under the falx. Often silent; may compress the anterior cerebral artery causing contralateral leg weakness. Midline shift on CT.
2 Uncal	Medial temporal lobe over the tentorial edge. Ipsilateral pupil dilates first, then ptosis and ophthalmoplegia; falling consciousness; contralateral (or Kernohan ipsilateral) hemiparesis. Can compress the PCA → occipital infarction.
3 Central	Diencephalon pushed down through the notch. Drowsiness, small reactive pupils, Cheyne–Stokes → mid-position fixed pupils, flexion then extension → pontine and medullary failure. Can tear perforators (Duret haemorrhages).
4 Tonsillar	Cerebellar tonsils into the foramen magnum. Neck stiffness, head tilt, bradycardia and hypertension, ataxic breathing, sudden apnoea — the most rapidly fatal.
Upward cerebellar	Posterior fossa mass, especially after over-drainage of a supratentorial EVD. Midbrain compression, downgaze, sudden deterioration.
5 External	Brain through a craniectomy or fracture. Tense flap; also watch for "sinking flap" syndrome later.

CT SIGNS OF IMPENDING HERNIATION

- Effacement of the basal (perimesencephalic) cisterns — the single most useful sign.
- Midline shift at the septum pellucidum; > 5 mm is significant in TBI guidelines.
- Entrapment of the contralateral temporal horn.
- Effaced fourth ventricle and quadrigeminal cistern in posterior fossa lesions.
- Loss of grey–white differentiation and sulcal effacement (diffuse oedema).
- Tonsillar descent below the foramen magnum on sagittal imaging.

C CASE IN PRACTICE — TALK AND DIE

A 28-year-old is struck on the temple, loses consciousness briefly, then talks normally in the emergency department. Three hours later he is drowsy with a dilating right pupil.

Resolution. A right extradural haematoma from a torn middle meningeal artery. The lucid interval reflects a compliant intracranial space filling until it decompensates. Immediate evacuation — not osmotherapy alone — determines survival.

3.7 The Cushing response and the first minutes

The Cushing response — hypertension, bradycardia and irregular breathing — is a brainstem reflex that raises arterial pressure to keep perfusing the brain as intracranial pressure approaches it. It is a late, pre-terminal sign, not an early warning.

What it means

- Brainstem ischaemia from compression or global perfusion failure.
- Often accompanied by widened pulse pressure and arrhythmias.
- The full triad is present in only a minority of herniating patients; its absence is not reassuring.

What not to do

- Do not treat the hypertension in isolation — it is defending the brain. Treat the pressure.
- Do not treat the bradycardia with atropine as a primary measure.
- Do not wait for it before acting on a pupil.

IMMEDIATE ACTIONS — ANY SUSPECTED HERNIATION

Seconds CALL

- Call your senior, neurosurgery and the scanner in the same breath.

Minutes PROTECT

- Airway and oxygenation; avoid hypotension (SBP < 100–110 mmHg is harmful in TBI).¹⁵
- Head up 30°, neck midline, loosen tube ties and collars.

Minutes TREAT DRIVERS

- Pain, agitation, ventilator dyssynchrony, fever, seizures, hypoxia, hypercapnia, hyponatraemia.

Now BRIDGE

- Osmotherapy and brief hyperventilation as a bridge to imaging and surgery — the rescue drill on [p. 35](#).

! THE POINT TO CARRY

- The pupil changes before the blood pressure does. A new anisocoria in a patient with a mass lesion is herniation until imaging says otherwise.
- Ataxic breathing or a newly absent gag means the process has reached the medulla — minutes, not hours.

E WHY SPEED MATTERS

Clinical herniation is reversible in a proportion of patients if relieved quickly, particularly with an expanding extra-axial haematoma. Outcome after evacuation of an acute subdural or extradural haematoma is strongly related to the interval between pupillary change and decompression — the classical neurosurgical observation behind every "time is brain" protocol for mass lesions. **OBS**

I NOT EVERY SURGE IS CUSHING — PAROXYSMAL SYMPATHETIC HYPERACTIVITY

After severe TBI or hypoxic injury, episodic tachycardia, hypertension, tachypnoea, hyperthermia, sweating and posturing — often triggered by handling — suggest paroxysmal sympathetic hyperactivity (PSH).¹⁶ Heart rate rises rather than falls; pupils and ICP are unchanged. Exclude seizures, sepsis, pain and withdrawal; treat with opioids, propranolol, gabapentin or clonidine, dosed before care.

4

CHAPTER FOUR

Raised intracranial pressure

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Explain compliance and autoregulation, and why perfusion — not the ICP number — is the target.
- Choose and interpret ICP monitoring, including waveform and non-invasive signs.
- Escalate treatment in SIBICC tiers and run the herniation rescue drill.

4.1 Monro–Kellie and compliance

The adult skull is a rigid box holding brain (about 80% of the volume), blood (about 10%) and CSF (about 10%). Because the total cannot change, any new volume must be matched by an equal loss elsewhere — the Monro–Kellie doctrine.¹⁷ **PHYSIOLOGY**

Early on, compensation works well: CSF moves into the spinal subarachnoid space and venous blood is squeezed out of the sinuses. Pressure barely changes, which is why a patient can carry a large mass and look deceptively well.

Once those buffers are exhausted the relationship becomes exponential. The same few millilitres that produced no change an hour ago now produce a steep rise. That is what **poor compliance** means at the bedside, and why deterioration in these patients is characteristically sudden.

Normal values: adult supine ICP 5–15 mmHg; transient rises with coughing and straining are normal in a compliant system.

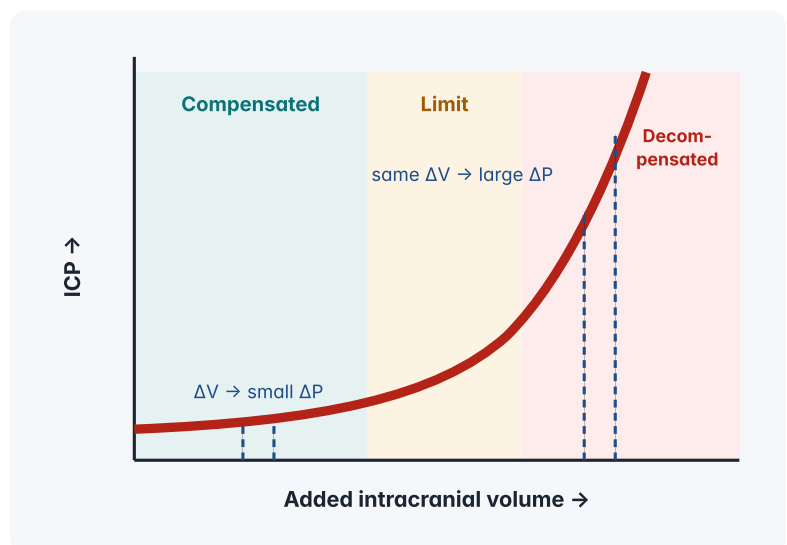


Figure 4.1 The pressure–volume curve. Original schematic.

CPP = MAP – ICP. You do not treat a number on a monitor — you defend the perfusion of tissue that has lost its ability to defend itself.

TWO BEDSIDE CONSEQUENCES OF POOR COMPLIANCE

Alert until suddenly not

A patient with a large mass may talk until the moment they herniate. "Talk and deteriorate" after head injury is the classic example, usually from an expanding extradural or subdural haematoma or contusion.

Small insults, large spikes

A bout of coughing, a tight collar, a brief seizure or a turn for a pressure-area check can produce disproportionate rises. Prevent spikes rather than react to them: pre-emptive analgesia and sedation before handling.

4.2 Autoregulation and cerebral perfusion

A healthy brain holds blood flow nearly constant across a range of perfusion pressures by changing arteriolar diameter. After injury this plateau narrows, shifts and may disappear, so that flow becomes passively dependent on blood pressure.^{17,18}

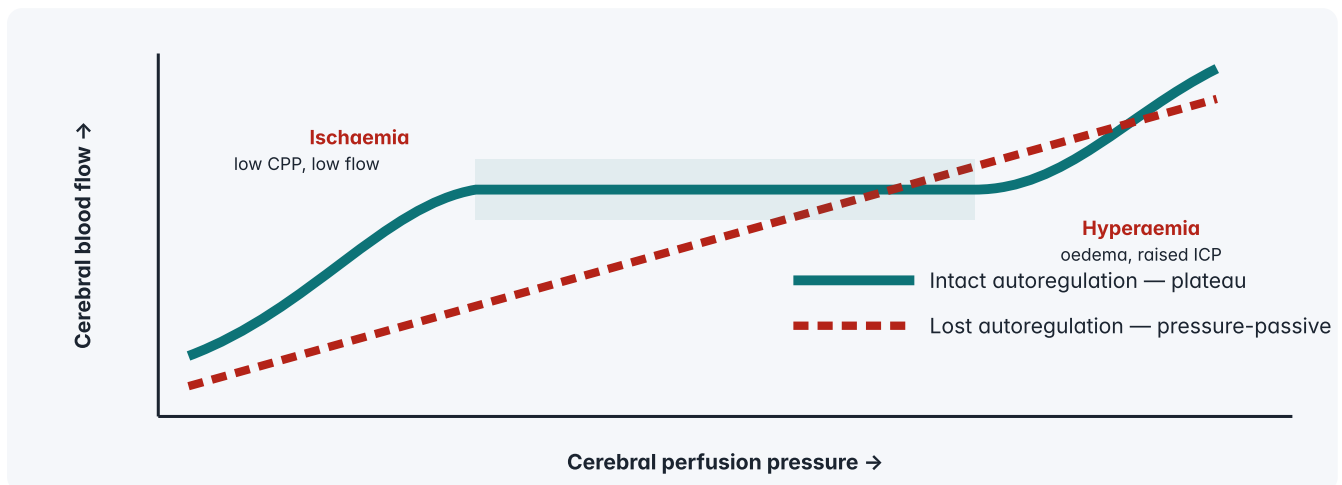


Figure 4.2 Cerebral autoregulation. The limits of the plateau vary between individuals and shift with chronic hypertension, injury and PaCO₂; the textbook range of 50–150 mmHg is an approximation. Original schematic.

WHAT IT MEANS AT THE BEDSIDE

- **Hypotension causes ischaemia.** A single episode of SBP < 90 mmHg after TBI is associated with substantially worse outcome.¹⁵
OBS
- **Hypertension causes hyperaemia** and vasogenic oedema in a pressure-passive bed.
- **CO₂ reactivity** is usually preserved longer than pressure autoregulation — the basis of hyperventilation, and of its danger.
- Keep transfers, turns and procedures haemodynamically quiet.

INDIVIDUALISING CPP — PRX AND CPP_{OPT}

The pressure reactivity index (PRx) is a moving correlation between slow waves of arterial pressure and ICP.¹⁸ When vessels react, a rise in MAP causes vasoconstriction and ICP falls or holds — PRx is negative or near zero. When they do not, ICP follows MAP passively — PRx is positive (above about +0.2 to +0.3 is commonly regarded as impaired).

Plotting PRx against CPP over hours gives a U-shaped curve whose minimum is the **optimal CPP**. Targeting CPP_{opt} rather than a fixed 60–70 mmHg is physiologically attractive and feasible, but its effect on outcome is not yet established.

INVESTIGATIONAL

★ TEACHING POINT

Most ICP you can control today is controlled by position, ventilation, temperature, sedation, seizure control and blood pressure — not by osmotherapy. Before every escalation ask: have I actually fixed the easy drivers?

© CASE IN PRACTICE — HYPOTENSION DURING TRANSFER

A patient with severe TBI and a CPP of 65 mmHg is transferred to CT. Propofol is given for agitation on the table; MAP falls to 55 mmHg for ten minutes. On return, ICP has risen from 18 to 30 mmHg.

Resolution. With impaired autoregulation, falling MAP causes vasodilatation and a rise in cerebral blood volume (the vasodilatory cascade), and ischaemia. Restoring MAP with a vasopressor brought ICP down. Transfers are ICP events — plan the sedation and the pressor before you move.

4.3 Monitoring — who, how and with what

ICP monitoring does not treat anything; it informs treatment. Its value lies in detecting what the examination cannot see in a sedated patient, and in guiding when to escalate and when to stop.¹⁹

INDICATIONS IN SEVERE TBI

- BTF 4th edition: management of severe TBI using information from ICP monitoring is recommended to reduce in-hospital and two-week mortality.¹⁵ **BTF IIB**
- Traditional criteria from the 3rd edition remain widely used: GCS 3–8 after resuscitation with an abnormal CT; or a normal CT with two or more of age > 40, motor posturing, or SBP < 90 mmHg. **BTF 3RD ED.**
- Outside TBI — SAH with hydrocephalus, ICH with intraventricular extension, fulminant hepatic failure, large infarcts — monitoring is individualised.

E BEST:TRIP — WHAT IT DID AND DID NOT SHOW

In 324 patients with severe TBI in Bolivia and Ecuador, a protocol guided by ICP monitoring was not superior to one guided by serial imaging and clinical examination.²⁰ **RCT** The trial tested a management *protocol*, not the value of information, in a setting without prehospital systems typical of high-income countries. Its practical lesson is that careful clinical and imaging surveillance is a legitimate strategy when monitoring is unavailable — not that monitoring is useless.

MONITORING DEVICES

Device	Strengths	Limitations
External ventricular drain	Reference standard; therapeutic CSF drainage; can be re-zeroed	Insertion into small or shifted ventricles; haemorrhage; ventriculitis; reads poorly while draining in most systems
Intraparenchymal transducer	Easy insertion; low infection and haemorrhage risk; continuous waveform	Cannot drain CSF; cannot be re-zeroed after insertion (drift); measures local pressure
Brain tissue oxygen (PbtO₂)	Detects hypoxia at normal ICP; SIBICC treatment threshold < 20 mmHg ²¹	Regional measurement; placement matters; outcome benefit under study
Subdural, epidural, lumbar	—	Less accurate; lumbar pressure unsafe with mass effect

I EVD ESSENTIALS

- Zero at the external auditory meatus (tragus) — a surrogate for the foramen of Monro; re-level after every position change.
- Most systems cannot drain and read at once — clamp to read, and know which mode you are in.
- A sudden loss of waveform is a blocked or displaced catheter until proven otherwise.
- Over-drainage can cause subdural collections and upward herniation in posterior fossa lesions.

I BEFORE YOU BELIEVE THE NUMBER

- Is the waveform physiological (pulsatile, with a respiratory swing)?
- Is the transducer at the right level and zeroed?
- Does the number fit the patient and the scan?
- A drifting or damped device has ended more than one unnecessary escalation.

4.4 Reading the waveform, and non-invasive signs

The ICP number is the mean of a waveform that contains more information than the number. Its shape reports on compliance before the mean has moved.¹⁷



Figure 4.3 The pulse waveform. P1, percussion wave (arterial pulse); P2, tidal wave (reflects brain compliance); P3, dicrotic wave (aortic valve closure). Original schematic.

SLOW WAVES (LUNDBERG)

Wave	Description and meaning
A (plateau)	Sustained rises to roughly 50–100 mmHg for 5–20 minutes in a poorly compliant brain, often triggered by vasodilatation. Pathological — treat the trigger and the pressure. ²²
B	Oscillations at 0.5–2 per minute; reflect vasomotor activity and limited reserve.
C	4–8 per minute, coupled to arterial (Traube–Hering–Mayer) waves; little clinical significance.

COMPLIANCE INDICES

RAP — the correlation between pulse amplitude and mean ICP — rises towards +1 as compliance is lost, and falls again when the vascular bed fails. It is used mainly in research and specialist centres.

WHEN THERE IS NO MONITOR

Signal	Use and limits
Serial examination	Pupils, motor score, FOUR B — still the backbone
CT	Cistern effacement, shift, sulcal effacement; a snapshot, not a trend
Optic nerve sheath diameter	Ultrasound 3 mm behind the globe. Values above roughly 5–6 mm suggest raised ICP; thresholds vary between studies, so trends in one patient are more useful than a single value. ²³
Transcranial Doppler	Rising pulsatility index and falling diastolic velocity suggest rising ICP; poor at estimating an absolute value
Pupillometry	Falling NPi can precede clinical change

1 NON-INVASIVE ≠ MONITORING

No non-invasive technique is accurate enough to titrate therapy against a threshold. Use them to triage, to decide who needs an invasive monitor, and to trend.

C CASE IN PRACTICE — THE NUMBER THAT WAS NOT REAL

An EVD reads 4 mmHg for six hours in a patient whose pupils have become sluggish. The trace is flat, without pulsatility.

Resolution. The catheter was blocked. A flat trace with a low number in a deteriorating patient is a device failure until proven otherwise. CT showed enlarging ventricles; the drain was flushed under aseptic conditions by neurosurgery and ICP read 34 mmHg.

4.5 Targets — and where each one comes from

Targets give a threshold for action. They are not interchangeable: each comes from a specific guideline, in a specific population — usually adults with severe traumatic brain injury. Apply them elsewhere with judgement.

Variable	Target	Source and level	Notes
ICP	Treat when > 22 mmHg	BTF 4th ed. ¹⁵ IIB	Values above this were associated with higher mortality; act on sustained rises, not brief spikes
CPP	60–70 mmHg	BTF 4th ed. IIB	The optimum may differ by patient (CPPopt)
CPP ceiling	Avoid driving CPP > 70 with fluids and vasopressors	BTF 4th ed. III	Risk of ARDS
Systolic BP	≥ 100 mmHg (age 50–69); ≥ 110 mmHg (15–49 or > 70)	BTF 4th ed. III	Pre-ICP-monitor phase especially
PaCO₂	35–45 mmHg baseline; 35–38 in Tier 1	SIBICC 2019 ²⁴ CONSENSUS	Prophylactic hyperventilation to ≤ 25 mmHg is not recommended (BTF IIB)
SpO₂	≥ 94%	SIBICC 2019 CONSENSUS	BTF identifies hypoxia (PaO ₂ < 60 mmHg, SpO ₂ < 90%) as harmful
PbtO₂	≥ 20 mmHg	SIBICC 2020 ²¹ CONSENSUS	Where monitored
Haemoglobin	> 7 g/dL	SIBICC 2019 CONSENSUS	Optimal threshold in brain injury debated
Sodium	Avoid hyponatraemia; during osmotherapy commonly 145–155 mmol/L	Common practice; NCS cerebral oedema guideline ²⁵	Not a BTF target; avoid > 160
Temperature	Prevent fever	SIBICC 2019 CONSENSUS	Prophylactic hypothermia not recommended (BTF IIB)
Glucose	Avoid hypo- and marked hyperglycaemia	General ICU practice	Commonly 140–180 mg/dL (7.8–10 mmol/L)

! NEVER IN TBI

- **Corticosteroids** to lower ICP or improve outcome. The CRASH trial (10 008 patients) found increased mortality with methylprednisolone. ²⁶ **RCT**
- **Prophylactic hyperventilation** to PaCO₂ ≤ 25 mmHg.

! STEROIDS ARE NOT BANNED EVERYWHERE

Dexamethasone remains effective for vasogenic oedema around tumours and abscesses, and in bacterial meningitis (**p. 43**). It has no role in cytotoxic oedema from stroke or hypoxic injury.

4.6 Tiered management — SIBICC

Tiers put reversible, low-risk measures first and reserve the high-risk ones for refractory pressure. The SIBICC consensus algorithm is the current reference for adults with severe TBI and an ICP monitor.²⁴ **CONSENSUS**

Tier	Interventions	Notes
Tier 0 everyone	Head of bed 30–45°; analgesia and sedation to prevent agitation and ventilator dyssynchrony; prevent fever; maintain CPP $\geq$ 60 mmHg initially; Hb $>$ 7 g/dL; avoid hyponatraemia; SpO ₂ $\geq$ 94%; PaCO ₂ 35–45 mmHg; optimise venous return; consider seizure prophylaxis for one week	Revisit at every escalation
Tier 1	CPP 60–70 mmHg; deepen analgesia and sedation; PaCO ₂ at the low end of normal (35–38 mmHg); mannitol by intermittent bolus (0.25–1 g/kg) or hypertonic saline bolus; CSF drainage if an EVD is present (or place one); consider EEG	Monitor sodium and osmolality
Tier 2	Mild hypocapnia (PaCO ₂ 32–35 mmHg); neuromuscular blockade trial in adequately sedated patients if efficacious; MAP challenge to assess autoregulation; raise CPP with fluids, vasopressors or inotropes when autoregulation is intact	Blockade hides seizures — EEG cover
Tier 3	Pentobarbital or thiopental coma titrated to ICP control (test dose first); secondary decompressive craniectomy; mild hypothermia (35–36 °C) with active cooling	Salvage — discuss goals of care alongside

HOW TO USE THE TIERS

- Tiers are not strictly sequential: you may skip a tier when the situation demands (for example, immediate surgery for a mass lesion).
- Within a tier, order is by local preference and patient factors, not ranking.
- Move up when ICP stays above threshold despite the current tier; move back down once control is sustained.
- Surgical lesions are evacuated at any tier — the algorithm assumes they have been dealt with.

NOT RECOMMENDED BY SIBICC

- Mannitol by continuous infusion, or scheduled hypertonic saline infusions to raise sodium.
- Lumbar CSF drainage.
- Routine PaCO₂ below 30 mmHg.
- Fluid loading or vasopressors to drive CPP $>$ 90 mmHg.
- Routine corticosteroids.

I BEFORE ESCALATING A TIER

- Re-check position, tube ties, collars, PaCO₂, temperature, pain, seizures and sodium.
- Confirm the monitor is reading correctly — zero, level, waveform.
- Re-image if the cause of the rise is not known: a new or expanding haematoma, hydrocephalus or infarct changes the plan.

E SIBICC FOR COMBINED ICP AND PbtO₂

A parallel algorithm addresses patients with both monitors, with four scenarios: both normal, ICP high with normal PbtO₂, PbtO₂ low with normal ICP, and both abnormal. Low PbtO₂ with normal ICP prompts measures to raise oxygen delivery — CPP, FiO₂, haemoglobin — rather than ICP-lowering therapy.²¹

4.7 The blown pupil — rescue drill

This page exists to be followed in order, under pressure. A new unilateral fixed dilated pupil in a patient with an intracranial mass means CN III is being compressed at the tentorial edge. Everything below buys time until the mass is removed or the pressure relieved — nothing here is definitive treatment.^{15,25}

0–60 s

RECOGNISE ·
CALL

- Confirm the pupil (size, reaction) and the conscious level. Call neurosurgery and your senior and alert CT **at the same time**, not one after the other.

Immediately

AIRWAY ·
POSITION

- Secure the airway if not already done; avoid both hypoxia and hypotension — each worsens outcome independently.
- Head up 30°, neck midline, loosen tube ties and remove a tight cervical collar if spinal precautions allow.

Bridge

VENTILATION

- Brief, controlled hyperventilation to PaCO₂ 30–35 mmHg, guided by blood gas or capnography.
- Temporary only — reverse once definitive treatment is under way; prolonged hypocapnia causes ischaemia.

Osmotherapy

LOWER VOLUME

- **23.4% NaCl 30 mL** over 10–20 minutes via a central line, *or* **3% NaCl 250 mL** (or 5 mL/kg) peripherally if no central access.
- *Or* **mannitol 20% 1 g/kg** (0.5–1.5 g/kg) — ensure the patient is not hypovolaemic; replace urine losses.
- Send sodium, osmolality, glucose and coagulation with the dose.

Seizures · sedation

REDUCE DEMAND

- Deepen sedation and analgesia; treat any seizure; consider neuromuscular blockade for coughing or dyssynchrony.

Definitive

SURGERY

- CT immediately, then evacuation, decompressive craniectomy or EVD as indicated.
- Reverse anticoagulation urgently — it changes the surgical option (**p. 41**).

! WHILE YOU DO ALL OF THIS

- Keep MAP up: hypotension in a herniating patient is lethal.
- No hypotonic or glucose-containing fluids.
- Osmotherapy without a surgical plan is delay, not treatment.

★ MEASURE THE RESPONSE

Re-examine the pupils every 5–10 minutes. Pupillary recovery after osmotherapy confirms a reversible compressive cause and supports urgent surgery; persistence despite treatment does not by itself mean futility.

✓ DRILL RECORD — WRITE IT AS YOU GO

- Time pupil change noticed · time neurosurgery called · time CT · time of osmotherapy and agent · PaCO₂ achieved · pupil response at 10 and 30 minutes · time to theatre.
- These times are the audit trail of a time-critical pathway and teach the team what went well.

4.8 Osmotherapy

Osmotic agents create a gradient across an intact blood–brain barrier and draw water out of brain tissue; mannitol also reduces blood viscosity, producing reflex vasoconstriction. Both agents lower ICP. They differ in their effect on circulating volume, which usually decides the choice.²⁵

NCS 2020

Agent	Dose	Monitor	Caution
Mannitol 20%	0.5–1 g/kg IV bolus over 15–20 min; up to 1.5 g/kg for herniation	Osmolar gap before each repeat dose — withhold if > 20 mOsm/kg (unexcreted mannitol). Serum osmolality ceiling of 320 is a weaker guide	Osmotic diuresis → hypovolaemia, hypotension; nephrotoxicity with accumulation; rebound oedema with prolonged use
Hypertonic saline 3%	250 mL (or 2–5 mL/kg) bolus	Sodium every 4–6 h	Volume expander — caution in heart failure; hyperchloraemic acidosis
Hypertonic saline 7.5%	~2 mL/kg via central line	Sodium	Central access preferred
Hypertonic saline 23.4%	30 mL over 10–20 min	Sodium; central access mandatory	Herniation rescue; never peripherally; hypotension with rapid push

Osmolar gap = measured osmolality – calculated osmolality, where calculated = $2 \text{ Na} + \text{glucose} + \text{urea}$ (all in mmol/L).

CHOOSING BETWEEN THEM

- **Hypovolaemic or hypotensive:** hypertonic saline — it expands volume rather than depleting it.
- **Volume overloaded or in heart failure:** mannitol, with attention to fluid balance and renal function.
- **Renal impairment:** favours hypertonic saline.
- **Established hypernatraemia (> 155–160):** favours mannitol.
- The NCS guideline suggests hypertonic saline may be considered over mannitol for ICP reduction in TBI; the difference in outcome is unproven.²⁵ **WEAK**

SAFE PRACTICE

- Give a defined bolus, then reassess ICP and sodium — repeated unmonitored dosing is how patients arrive at a sodium of 165.
- Sodium, osmolality and renal function at least every 6 hours during active treatment.
- Do not lower sodium quickly when stopping — a rapid fall can provoke rebound cerebral oedema; aim for a slow decline.
- Hypertonic saline in chronic hyponatraemia risks osmotic demyelination — know the baseline sodium.

1 A COMMON ERROR

An osmolar gap above 20 mOsm/kg means mannitol is accumulating — a reason to **withhold** the next dose, not a target to reach.

WORKED EXAMPLE — THE OSMOLAR GAP

Measured osmolality 318 mOsm/kg · Na 146 · glucose 7 · urea 6 (mmol/L).

Calculated = $2 \times 146 + 7 + 6 = 305$. Gap = $318 - 305 = 13$ → mannitol is being cleared; the next dose can be given if indicated.

If measured osmolality were 330, the gap would be 25 → **withhold**.

4.9 Hyperventilation, surgery, hypothermia and barbiturates

These are the high-risk tools. Each has trial evidence that defines both its benefit and its cost.

HYPERVENTILATION

Works by cerebral vasoconstriction — which is exactly why it is dangerous if sustained. Reserve for acute herniation as a bridge (PaCO₂ 30–35 mmHg) and Tier 2 mild hypocapnia (32–35 mmHg), ideally with PbtO₂ or jugular venous oxygen monitoring. Avoid prophylactic hyperventilation to ≤ 25 mmHg, especially in the first 24 hours when flow is already low.¹⁵ Reverse gradually: abrupt normalisation causes rebound hyperaemia.

BARBITURATE COMA

High-dose barbiturates reduce cerebral metabolism and ICP. BTF recommends them for refractory raised ICP after maximal standard medical and surgical therapy, with haemodynamic stability — never prophylactically.¹⁵ **BTF IIB** Expect hypotension, immunosuppression, ileus and a prolonged, uninterpretable clinical examination; titrate with EEG.

NEUROMUSCULAR BLOCKADE

Abolishes coughing and dyssynchrony. Give a test dose and observe the ICP response; continue only if effective. It removes the motor examination and hides seizures — continuous EEG is advisable.

E DECOMPRESSIVE CRANIECTOMY

DECRA — early bifrontal craniectomy for moderate, early ICP elevation in diffuse TBI lowered ICP but worsened functional outcome.²⁷

RCT

RESCUEicp — secondary craniectomy for refractory ICP > 25 mmHg reduced mortality at six months, at the cost of more survivors in vegetative state or with severe disability.²⁸ **RCT**

BTF 2020 update: secondary craniectomy is recommended for late refractory ICP elevation to improve mortality and favourable outcome; a large fronto-temporo-parietal flap (not less than 12 × 15 cm or 15 cm diameter) is recommended over a small one.²⁹ **BTF IIA**

E HYPOTHERMIA

Eurotherm3235 — hypothermia to 32–35 °C as a Tier 2 ICP measure lowered ICP but produced worse functional outcome.³⁰ **RCT** **SIBICC** therefore places only mild hypothermia (35–36 °C) in Tier 3. Fever prevention is the routine target.

★ TEACHING POINT

Lowering ICP and improving outcome are different things. Surgery and hypothermia can achieve the first while worsening the second — which is why goals of care belong in every Tier 3 conversation.

TIER 3 OPTIONS COMPARED

Option	ICP effect	Outcome evidence	Main cost
Secondary craniectomy	Large and immediate	Lower mortality, more severe disability (RESCUEicp)	Surgery, cranioplasty, hygroma, hydrocephalus
Barbiturate coma	Moderate; variable responders	No proven outcome benefit	Hypotension, infection, loss of examination
Mild hypothermia 35–36 °C	Modest	Deeper hypothermia harmful (Eurotherm)	Infection, coagulopathy, shivering

5

CHAPTER FIVE

Disease-specific management

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Apply the first-day priorities for TBI, aneurysmal SAH, ICH and severe ischaemic stroke.
- Start time-critical treatment for CNS infection and neuromuscular respiratory failure.
- Distinguish SIADH from cerebral salt wasting and correct sodium safely.

5.1 Traumatic brain injury — the first day

The primary injury happens at impact. Everything the ICU does is aimed at secondary injury — hypoxia, hypotension, raised ICP, seizures, fever and hyponatraemia — which is preventable.¹⁵

Severity	GCS after resuscitation
Mild	13–15
Moderate	9–12
Severe	3–8

PRIORITIES

- **Oxygen and pressure:** avoid SpO₂ < 90% and SBP below the age-specific threshold (p. 33).
- **Surgical lesions first:** extradural, acute subdural and contusions with mass effect go to theatre before ICP algorithms begin.
- **Repeat CT** at 6–24 h or with any deterioration — contusions expand ("blossom"), especially with coagulopathy.
- **Reverse anticoagulation** promptly; check platelets and fibrinogen.

E TRANEXAMIC ACID — CRASH-3

In 12 737 patients with TBI and intracranial bleeding (or GCS ≤ 12) treated within 3 hours, tranexamic acid (1 g over 10 min, then 1 g over 8 h) reduced head-injury death in mild-to-moderate TBI; no clear benefit was seen in severe TBI or with bilaterally unreactive pupils. Earlier treatment was more effective.³¹ RCT

RECOMMENDATIONS FROM BTF 4TH EDITION

- Seizure prophylaxis for 7 days to prevent early post-traumatic seizures; phenytoin has the evidence (IIA), levetiracetam is widely used as an alternative with insufficient comparative evidence. Prophylaxis does not prevent late epilepsy.
- Basal caloric replacement by day 5, at most day 7 (IIA).
- Pharmacological VTE prophylaxis once the haemorrhage is stable (III).
- Steroids are not recommended (I).

★ TEACHING POINT

A patient who talks and then deteriorates has a surgical lesion until proven otherwise. CT before ICU admission, and again before any escalation of medical therapy.

MARSHALL CT CLASSIFICATION OF DIFFUSE INJURY³²

Category	Definition
Diffuse injury I	No visible intracranial pathology on CT
Diffuse injury II	Cisterns present; midline shift 0–5 mm; no high- or mixed-density lesion > 25 mL
Diffuse injury III (swelling)	Cisterns compressed or absent; shift 0–5 mm; no lesion > 25 mL
Diffuse injury IV (shift)	Midline shift > 5 mm; no lesion > 25 mL
Evacuated mass lesion (V)	Any lesion surgically evacuated
Non-evacuated mass lesion (VI)	High- or mixed-density lesion > 25 mL, not evacuated

5.2 Aneurysmal subarachnoid haemorrhage — grading and the first 72 hours

Aneurysmal SAH has three phases with different threats: rebleeding in the first hours, hydrocephalus and brain injury from the ictus, and delayed cerebral ischaemia from day 3 to day 14. The 2023 AHA/ASA guideline is the reference.³³ [AHA 2023](#)

WFNS GRADE³⁴

Grade	GCS	Motor deficit
I	15	Absent
II	13–14	Absent
III	13–14	Present
IV	7–12	Present or absent
V	3–6	Present or absent

HUNT AND HESS GRADE³⁵

Grade	Clinical picture
1	Asymptomatic or mild headache, slight nuchal rigidity
2	Moderate–severe headache, nuchal rigidity, no deficit other than cranial nerve palsy
3	Drowsy, confused or mild focal deficit
4	Stupor, moderate–severe hemiparesis
5	Deep coma, decerebrate posturing, moribund

MODIFIED FISHER SCALE — RISK OF VASOSPASM AND DCI³⁶

Grade	CT finding	Approximate risk of symptomatic vasospasm
0	No SAH or IVH	Very low
1	Thin SAH, no IVH	About 1 in 4
2	Thin SAH with IVH	About 1 in 3
3	Thick SAH, no IVH	About 1 in 3
4	Thick SAH with IVH	About 2 in 5

BEFORE THE ANEURYSM IS SECURED

- **Secure early** — clipping or coiling as soon as feasible, ideally within 24 hours, to prevent rebleeding.
- **Blood pressure:** treat marked hypertension to lower rebleeding risk; a systolic below about 160 mmHg is common practice, though the ideal target is unknown.
- **Antifibrinolytics** do not improve functional outcome and are not recommended for that purpose.
- **Reverse anticoagulation;** analgesia; stool softeners.

HYDROCEPHALUS AND SEIZURES

- Acute hydrocephalus with a reduced conscious level → urgent EVD. Expect improvement in grade after drainage — grade the patient again before prognosticating.
- Routine long-term antiseizure prophylaxis is not recommended; phenytoin prophylaxis is associated with worse outcome. A short course in the early period may be considered.
- Clinical seizures, or unexplained poor grade, merit EEG.

C CASE IN PRACTICE — THE GRADE THAT CHANGED

A 52-year-old arrives with a thunderclap headache and GCS 6 — WFNS V. The family is told the outlook is grave. CT shows a thick SAH and dilated ventricles.

Resolution. After an EVD, GCS rises to 12 within hours — now WFNS IV. The aneurysm is coiled the same day. Grade on admission reflected hydrocephalus as much as brain injury; prognosis was revised only after the reversible component was treated.

5.3 SAH — delayed cerebral ischaemia and the ICU phase

Delayed cerebral ischaemia (DCI) is new focal deficit or a fall in GCS of at least two points lasting an hour or more, not explained by another cause, typically between days 3 and 14. Angiographic vasospasm is common; DCI is the clinical event that matters.³³

PREVENT

- **Nimodipine 60 mg orally or by tube every 4 hours for 21 days.** If it causes hypotension, give 30 mg every 2 hours. RCT
- Maintain **euvolaemia**. Prophylactic hypervolaemia and prophylactic induced hypertension ("triple-H") are not recommended.
- Avoid hyponatraemia and fever; maintain normoglycaemia.
- Intravenous magnesium and statins have not improved outcome and are not recommended for this purpose.

DETECT

- Serial neurological examination is the primary monitor in good-grade patients.
- Transcranial Doppler — rising velocities and Lindegaard ratio — or CT angiography and perfusion in poor-grade patients whose examination is limited.
- Continuous EEG with quantitative trends can detect ischaemia early in specialist centres.

TREAT

- Exclude rebleeding, hydrocephalus, seizures, hyponatraemia, hypoxia and infection.
- **Induced hypertension** with vasopressors, in a secured aneurysm, is reasonable for symptomatic DCI; reassess the deficit against each step in MAP.
- Refractory cases: endovascular rescue — intra-arterial vasodilators and/or angioplasty.

! SODIUM AFTER SAH

Hyponatraemia is common and is often cerebral salt wasting rather than SIADH. **Do not fluid-restrict** a patient after SAH — volume depletion increases the risk of DCI. Use isotonic or hypertonic saline, and consider fludrocortisone for natriuresis ([p. 45](#)).

★ TEACHING POINT

A good-grade patient who becomes drowsy on day 6 has DCI until proven otherwise. Examine, check sodium and the drain, image the vessels, and raise the pressure while you look.

OTHER ICU COMPLICATIONS TO ANTICIPATE

Complication	Recognition and response
Neurogenic stunned myocardium	Troponin rise, regional wall-motion abnormality not in a coronary territory, pulmonary oedema; usually reversible. Inotropes rather than pure vasoconstrictors if output is low.
Neurogenic pulmonary oedema	Early hypoxaemia after poor-grade SAH; lung-protective ventilation, avoid fluid overload but not at the cost of hypovolaemia.

TRANSCRANIAL DOPPLER AFTER SAH — MIDDLE CEREBRAL ARTERY

Finding	Usual interpretation
Mean velocity < 120 cm/s	Vasospasm unlikely
120–200 cm/s	Possible to moderate vasospasm — interpret with the Lindegaard ratio
> 200 cm/s	Severe vasospasm likely
Lindegaard ratio (MCA / extracranial ICA)	> 3 suggests vasospasm rather than hyperaemia; > 6 severe

5.4 Spontaneous intracerebral haemorrhage

About a third of patients with ICH show haematoma expansion in the first hours, and expansion predicts death and disability. Early management is about stopping growth: blood pressure, reversal of anticoagulation, and selecting patients for surgery.³⁷ **AHA 2022**

BLOOD PRESSURE

- For mild-to-moderate ICH presenting with SBP 150–220 mmHg, lowering to a target of 140 mmHg, keeping it within 130–150 mmHg, is safe and may improve functional outcome.
- Lowering SBP below 130 mmHg in this group is potentially harmful.
- Start early, titrate smoothly and avoid large variability — infusions (labetalol, nicardipine, clevidipine) beat repeated boluses.

WHO NEEDS SURGERY

- Cerebellar ICH** with neurological deterioration, brainstem compression or hydrocephalus — evacuate, not EVD alone.
- Intraventricular haemorrhage with hydrocephalus — EVD.
- Supratentorial ICH — selected patients only; minimally invasive evacuation is an evolving option in specialist centres.

REVERSAL OF ANTITHROMBOTICS

Agent	Reversal
Warfarin (INR ≥ 2)	4-factor PCC (dose by INR and weight) plus vitamin K 10 mg IV. PCC is preferred over plasma.
Dabigatran	Idarucizumab 5 g IV
Apixaban, rivaroxaban	Andexanet alfa, or 4-factor PCC (commonly 50 IU/kg) where andexanet is unavailable
Unfractionated heparin	Protamine 1 mg per 100 units given in the previous 2–3 hours
Antiplatelets	Platelet transfusion is not recommended unless neurosurgery is planned (harm in PATCH)

Doses per AHA 2022 and product labelling; confirm against your formulary.³⁷

THE ICH SCORE³⁸

Component	Points	Component	Points
GCS 3–4 / 5–12 / 13–15	2 / 1 / 0	Infratentorial origin	1
Volume ≥ 30 mL (ABC/2)	1	Age ≥ 80 years	1
Intraventricular extension	1	30-day mortality in derivation cohort: 0 → 0%; 1 → 13%; 2 → 26%; 3 → 72%; 4 → 97%; 5 → 100%	

! THE SELF-FULFILLING PROPHECY IN ICH

The ICH score was derived in a cohort in which care was often withdrawn early. It describes risk in a population and should not be used alone to limit treatment. Full care for at least the first day, with a reassessment before any withdrawal decision, is the safer default.

HAEMATOMA VOLUME — ABC/2

On the slice with the largest haematoma, measure the longest diameter (A) and the perpendicular diameter (B), in cm. Count the slices with haemorrhage and multiply by slice thickness (C, in cm). Volume ≈ A × B × C ÷ 2, in mL. Accurate for ellipsoid haematomas; overestimates irregular and anticoagulant-related ones. A CTA "spot sign" marks active extravasation and a high risk of expansion.

5.5 Severe ischaemic stroke in the ICU

Three ischaemic stroke syndromes regularly reach the ICU: basilar artery occlusion, malignant middle cerebral artery infarction, and space-occupying cerebellar infarction. Each has a time-critical intervention.³⁹

Basilar artery occlusion

Presents with fluctuating or falling consciousness, gaze palsies, skew, dysarthria, bilateral or crossed weakness and extensor plantars — sometimes preceded by days of "TIAs". It is easily misattributed to sedation, intoxication or a metabolic cause.

Act: CT angiography of the posterior circulation in any unexplained coma with brainstem signs; involve the stroke team immediately.

E THROMBECTOMY WORKS

ATTENTION (within 12 h) and **BAOCHE** (6–24 h) showed better functional outcome with endovascular thrombectomy than medical therapy alone in patients with moderate-to-severe deficits.^{40,41} RCT

Malignant MCA infarction

- Large territory infarct with oedema peaking at 2–5 days; falling consciousness and herniation.
- **Decompressive hemicraniectomy within 48 hours** in patients aged 60 or under roughly halves mortality and increases the proportion surviving with moderate disability.⁴² POOLED RCT
- Over 60, surgery improves survival but most survivors are dependent — discuss values with the family before, not after.
- Osmotherapy and hyperventilation are bridges only.

Cerebellar infarction

- Swelling compresses the fourth ventricle and brainstem, typically on days 2–4.
- Watch for falling consciousness, new gaze palsy, hydrocephalus.
- **Suboccipital decompressive craniectomy** for deterioration despite medical therapy; EVD alone risks upward herniation.³⁹
- Outcome after surgery is often good — this is not a lesion to give up on.

GENERAL ICU PRIORITIES AFTER ISCHAEMIC STROKE

- After thrombolysis, keep BP below 180/105 mmHg for 24 hours; avoid aggressive lowering after successful thrombectomy.
- Treat fever and hyperglycaemia; screen swallow before oral intake; early mobilisation when safe.
- Haemorrhagic transformation after reperfusion: stop antithrombotics, check coagulation, image, and consider cryoprecipitate if within 24 hours of thrombolysis.

★ TEACHING POINT

A patient on the ventilator for an unrelated reason who has "not woken" and has a new gaze palsy has a basilar occlusion until a CTA says otherwise.

5.6 Central nervous system infection and encephalitis

Bacterial meningitis kills through delay. Antibiotics and dexamethasone must not wait for imaging or lumbar puncture when the diagnosis is suspected.⁴³ ESCMID 2016

BACTERIAL MENINGITIS — THE FIRST HOUR

1. Blood cultures.
2. CT before LP **only** if focal deficit (other than CN palsies), new seizures, GCS < 10, or severe immunocompromise — and if CT comes first, treatment comes first too.
3. **Dexamethasone 10 mg IV every 6 hours for 4 days**, starting with or just before the first antibiotic dose. Stop if the organism is not *S. pneumoniae* or *H. influenzae*. RCT
4. **Empirical antibiotics**: ceftriaxone 2 g every 12 h (or cefotaxime) **plus** vancomycin where pneumococcal cephalosporin resistance is a concern **plus** amoxicillin/ampicillin 2 g every 4 h if *Listeria* risk (age > 50, immunocompromise, pregnancy, alcohol dependence). Follow local resistance patterns.

VIRAL ENCEPHALITIS

Start **aciclovir 10 mg/kg IV every 8 hours** (adjust for renal function; hydrate) in any suspected encephalitis until HSV PCR is negative — and repeat a negative PCR taken in the first 72 hours if suspicion remains. Treat confirmed HSV for 14–21 days.

AUTOIMMUNE ENCEPHALITIS

Possible autoimmune encephalitis (Graus criteria) requires all three:⁴⁴

1. Subacute onset (< 3 months) of working-memory deficits, altered mental status or psychiatric symptoms;
2. At least one of: new focal CNS findings, unexplained seizures, CSF pleocytosis, or MRI features suggesting encephalitis;
3. Reasonable exclusion of alternative causes.

Send serum and CSF antibodies, but do not wait for them: once infection is reasonably excluded, start first-line immunotherapy (high-dose methylprednisolone, IVIg or plasma exchange). Screen for tumour — ovarian teratoma in anti-NMDA receptor encephalitis.

! RED FLAGS IN THE ENCEPHALOPATHIC ICU PATIENT

- Fever, neck stiffness or rash with a falling GCS — treat for meningitis now.
- Orofacial dyskinesias, autonomic instability and refractory seizures in a young patient — anti-NMDA receptor encephalitis.
- New-onset refractory status epilepticus without a cause — investigate for autoimmune and paraneoplastic encephalitis early (p. 52).

CSF PATTERNS — TYPICAL, NOT ABSOLUTE

	Opening pressure	Cells (/μL)	Protein	Glucose ratio	Notes
Bacterial	High	Hundreds to thousands, neutrophils	High	< 0.4	Gram stain, culture, PCR; lactate high
Viral	Normal–mild	10–500, lymphocytes	Normal–mild	Normal	Early neutrophils possible
Tuberculous	High	50–500, lymphocytes	Very high	Low	Subacute; basal enhancement; hyponatraemia
Fungal	Very high	Lymphocytes, may be low	High	Low	Cryptococcal antigen; India ink

5.7 Neuromuscular respiratory failure

Neuromuscular respiratory failure is a ventilatory pump failure. Gas exchange stays normal until late; hypercapnia and hypoxaemia are pre-terminal signs. Decide on airway support from mechanics and bulbar function, not from the blood gas.

BEDSIDE MEASURES AND THE 20/30/40 RULE

Measure	Concerning value
Vital capacity	< 20 mL/kg, or a fall of more than 30% from baseline
Negative inspiratory force (NIF)	Weaker than -30 cmH ₂ O
Maximal expiratory pressure	< 40 cmH ₂ O
Single-breath count	< 20

Use a face mask if facial weakness prevents a lip seal. Trends over hours matter more than single values.

CLINICAL SIGNS OF IMPENDING FAILURE

- Tachypnoea, rapid shallow breathing, use of accessory muscles.
- **Paradoxical abdominal movement** — diaphragmatic weakness.
- Weak cough, pooled secretions, nasal speech, inability to count aloud — bulbar weakness.
- Neck flexor weakness tracks diaphragmatic weakness.

Guillain-Barré syndrome

- About a fifth to a quarter need ventilation.
- Predictors: rapid progression, bulbar and neck weakness, inability to lift elbows or head, falling VC.
- **IVIg 0.4 g/kg/day for 5 days** or plasma exchange, within 2 weeks of onset in patients unable to walk.⁴⁵ [EAN/PNS 2023](#)
- Dysautonomia: arrhythmias, labile BP; avoid suxamethonium (hyperkalaemia).
- Non-invasive ventilation is generally unsafe with bulbar weakness.

Myasthenic crisis

- Triggers: infection, surgery, drugs (aminoglycosides, fluoroquinolones, macrolides, magnesium, β -blockers), steroid initiation.
- **IVIg or plasma exchange**; then high-dose steroids.⁴⁶
- BiPAP may avert intubation if started before hypercapnia.
- Hold pyridostigmine while intubated (secretions).

! INTUBATE EARLY, ELECTIVELY

Do not wait for hypercapnia, hypoxaemia or fatigue. Elective intubation in a monitored setting is far safer than a crash intubation of an exhausted patient with secretions in the airway. Avoid suxamethonium in GBS and in any patient with denervation; non-depolarising agents need reduced doses in myasthenia.

WEAKNESS IN THE ICU — THREE COMMON CAUSES

	Guillain-Barré	Myasthenic crisis	ICU-acquired weakness
Onset	Days to 4 weeks, ascending	Hours to days, fatigable	After sepsis, steroids, immobility
Reflexes	Absent or reduced	Normal	Reduced
Bulbar / ocular	Facial and bulbar common; ocular in Miller Fisher	Ptosis, diplopia, bulbar prominent	Facial and ocular spared
Sensation	Often involved	Normal	Distal loss in polyneuropathy
Key test	CSF protein; nerve conduction	AChR / MuSK antibodies; repetitive stimulation	Nerve conduction, EMG, CK

5.8 Sodium disorders in the brain-injured patient

Sodium is the main determinant of serum osmolality and therefore of water movement across the blood–brain barrier. In brain injury, hyponatraemia worsens oedema and seizures, and hypernatraemia can be either therapy or diabetes insipidus.⁴⁷

HYPONATRAEMIA: SIADH OR CEREBRAL SALT WASTING?

Feature	SIADH	Cerebral salt wasting
Extracellular volume	Normal or mildly increased	Decreased — the defining feature
Urine sodium	> 30 mmol/L	> 30 mmol/L, often very high
Urine output	Normal or low	High
Fluid balance	Positive or even	Negative
Haematocrit, urea	Normal or low	Rising
Treatment	Fluid restriction (not after SAH); salt; hypertonic saline if symptomatic	Replace salt and volume — isotonic or hypertonic saline; fludrocortisone

Volume status is hard to judge at the bedside. When in doubt in a brain-injured patient, avoid fluid restriction.

CORRECTING HYPONATRAEMIA SAFELY

- **Severe symptoms** (seizures, falling GCS): 150 mL of 3% saline over 20 minutes; recheck sodium; repeat up to twice until sodium has risen by about 5 mmol/L.⁴⁷ **EUROPEAN 2014**
- **Limit** the rise to 10 mmol/L in the first 24 hours and 8 mmol/L in each following 24 hours.
- High risk of osmotic demyelination: alcohol use disorder, malnutrition, hypokalaemia, liver disease, sodium < 120 — aim lower.
- Overshoot: re-lower with free water and desmopressin under specialist guidance.

HYPERNATRAEMIA AND DIABETES INSIPIDUS

- Suspect central DI with polyuria (often > 250–300 mL/h for 2 hours), dilute urine (osmolality < 300 mOsm/kg) and rising sodium.
- Common after pituitary surgery, severe TBI, SAH — and in death by neurological criteria.
- Treat with desmopressin (for example 1–2 µg IV or SC) and replace the free-water deficit.
- Therapeutic hypernatraemia during osmotherapy is intended; distinguish it from DI by urine output and concentration.

★ TEACHING POINT

In the brain-injured patient, hyponatraemia is never benign. Measure sodium at least daily — every 6 hours on osmotherapy — and investigate any fall of more than 5 mmol/L.

WORKED EXAMPLE — FREE-WATER DEFICIT

A 70 kg man with diabetes insipidus has a sodium of 156 mmol/L. Total body water $\approx 0.6 \times 70 = 42$ L. Free-water deficit = $42 \times (156 \div 140 - 1) \approx 4.8$ L. Replace over 24–48 hours (lower sodium by no more than about 10 mmol/L per day in chronic hypernatraemia), add ongoing urine losses, and give desmopressin to stop them.

© CASE IN PRACTICE — SALT WASTING AFTER SAH

On day 5 after coiling, sodium falls from 139 to 129 mmol/L over 48 hours. Urine output is 4 L/day, the fluid balance is –1.8 L and urea is rising. The team considers fluid restriction for "SIADH".

Resolution. The volume picture is cerebral salt wasting. Isotonic saline with 3% boluses and fludrocortisone restored sodium and balance; fluid restriction in the DCI window would have raised the risk of ischaemia.

6

CHAPTER SIX

Conditions that hide the examination

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Measure sedation and delirium with RASS and CAM-ICU.
- Choose sedatives with their neurological consequences in mind, and run a safe sedation hold.
- Recognise the drug and metabolic states that mimic structural brain injury.

6.1 Measuring sedation and delirium

Sedation is the commonest reason an ICU neurological examination is uninterpretable. Every agent suppresses arousal by acting on the system described on p. 10 — so the drug chart is part of the neurological assessment.⁴⁸

RICHMOND AGITATION-SEDATION SCALE⁴⁹

Score	Description
+4	Combative — immediate danger to staff
+3	Very agitated — pulls tubes, aggressive
+2	Agitated — frequent non-purposeful movement, fights ventilator
+1	Restless — anxious, movements not aggressive
0	Alert and calm
-1	Drowsy — sustained awakening to voice, eye contact $\geq$ 10 s
-2	Light sedation — briefly awakens to voice, eye contact < 10 s
-3	Moderate — movement or eye opening to voice, no eye contact
-4	Deep — no response to voice, movement to physical stimulation
-5	Unroutable — no response to voice or physical stimulation

CAM-ICU

Delirium is present when features **1 and 2** are present, plus **either 3 or 4**. It can be assessed only at RASS -3 or lighter.⁵⁰

1. Acute change or fluctuating course of mental status.
2. Inattention (e.g. squeezes on the letter "A" in a 10-letter sequence; $\geq$ 3 errors).
3. Altered level of consciousness (RASS other than 0).
4. Disorganised thinking.

DELIRIUM IN BRAIN INJURY

In a patient with a structural lesion, "delirium" may be the lesion, a seizure, hydrocephalus or a new event. A new fluctuation in a brain-injured patient is a neurological change first and delirium second.

E ABCDEF BUNDLE

Assess, prevent and manage pain · Both spontaneous awakening and breathing trials · Choice of analgesia and sedation · Delirium: assess, prevent, manage · Early mobility · Family engagement. PADIS recommends light sedation for most patients and non-pharmacological delirium prevention.⁴⁸ PADIS 2018

1 RASS IS NOT A NEUROLOGICAL SCORE

A RASS of -5 in a patient on no sedation is coma, not deep sedation. Always chart the RASS beside the drug and dose running, so the next reader can tell which they are looking at.

6.2 Analgosedation and the sedation hold

The ideal neuro-ICU sedative lowers ICP and metabolic demand, preserves the ability to examine, and does not drop the blood pressure. None does all three; choose deliberately.⁴⁸

Agent	Advantages	Neurological catch
Propofol	Rapid on and off — permits frequent examination; lowers ICP and CMRO ₂ ; antiseizure	Hypotension lowers CPP. Propofol infusion syndrome with high doses (above about 4 mg/kg/h) for longer than 48 h — watch lactate, CK, triglycerides, ECG, rising vasopressor needs.
Dexmedetomidine	Rousable sedation; less delirium; no respiratory depression	Bradycardia and hypotension; does not lower ICP or suppress seizures; insufficient alone for raised ICP or SE
Midazolam	Antiseizure; haemodynamically gentler	Accumulates in renal and hepatic failure and in obesity; prolonged coma that mimics a poor examination; delirium
Fentanyl, remifentanyl	Analgesia-first strategy; blunt cough and ICP spikes	Fentanyl accumulates with prolonged infusion; remifentanyl offsets fast but hyperalgesia on withdrawal; small pupils
Ketamine	Preserves BP; NMDA antagonist; useful in refractory SE	Historical concern over ICP is not borne out with controlled ventilation; nystagmus and roving eyes confound the examination
Barbiturates	Most potent ICP and metabolic suppression	Very long context-sensitive half-life; can abolish all brainstem reflexes for days

THE SEDATION HOLD — DOING IT SAFELY

- **Do not hold** during active intracranial hypertension, status epilepticus, neuromuscular blockade, or severe refractory hypoxaemia.
- Otherwise interrupt daily, paired with a spontaneous breathing trial, and examine at the moment of best wakefulness.
- With an ICP monitor, a sustained rise above threshold ends the hold.
- **Chart the examination at the trough of sedation** — that is the examination that means something.

WHEN THE PATIENT DOES NOT WAKE

If the patient does not wake as expected after an adequate washout, that is now a finding. Work through:

- Drug accumulation — renal and hepatic function, obesity, interacting drugs; levels where available.
- NCSE — EEG (p. 49).
- A new structural event — repeat CT.
- Metabolic causes — sodium, glucose, ammonia, CO₂, urea.
- Residual neuromuscular blockade — train-of-four.

★ BEFORE THE FAMILY MEETING

Every sedative charted today is a confounder you must clear before prognosticating. Record the drug, the dose and the time it was stopped. The washout — not the clock — decides when the examination becomes valid.

© CASE IN PRACTICE — NOT WAKING ON DAY 5

After six days of midazolam and fentanyl for ARDS, a patient with a small traumatic SAH remains RASS −4 48 hours after both were stopped. Brainstem reflexes are intact; creatinine is three times baseline.

Resolution. Accumulated midazolam metabolites and fentanyl; cEEG showed diffuse slowing without seizures. She woke on day 8. Until then the examination was documented as "confounded" and no prognosis was given.

6.3 Toxic and metabolic mimics of structural injury

The states below can produce coma with abnormal pupils, absent reflexes or posturing, and are reversible. Most are common in the ICU population.¹

Cause	Examination clues	Confirm and treat
Opioids	Pinpoint reactive pupils, hypoventilation	Naloxone in titrated doses (0.04–0.1 mg) to avoid abrupt withdrawal
Benzodiazepines	Small–normal reactive pupils, hypotonia	Washout; flumazenil rarely and never in benzodiazepine dependence or seizure risk
Baclofen	Coma, flaccidity, absent reflexes, bradycardia, seizures; can mimic brain death	Renal failure or intrathecal overdose; supportive care, haemodialysis
Anticholinergic	Large pupils, dry flushed skin, tachycardia, urinary retention	Withdraw drug; physostigmine in selected cases with toxicology advice
Serotonin syndrome	Clonus (inducible, ocular), hyperreflexia, hyperthermia, mydriasis	Stop serotonergic drugs; cooling; cyproheptadine
Neuroleptic malignant syndrome	Lead-pipe rigidity, hyperthermia, autonomic instability, raised CK	Stop antipsychotic; cooling; dantrolene or bromocriptine
Cefepime neurotoxicity	Encephalopathy, myoclonus, NCSE in renal impairment	EEG; stop or reduce cefepime; dialysis in severe cases
Valproate hyperammonaemia	Encephalopathy with normal liver tests	Ammonia; carnitine; stop valproate
Lithium	Tremor, myoclonus, coma, NCSE-like EEG	Level; haemodialysis for severe toxicity
Hepatic encephalopathy	Asterixis, hyperreflexia, can posture; pupils reactive	Ammonia (supportive, not diagnostic); lactulose, rifaximin; cerebral oedema in acute liver failure
Uraemia	Myoclonus, asterixis, seizures	Dialysis
Hypercapnia	Headache, drowsiness, asterixis, papilloedema	Blood gas; ventilatory support
Hypo- and hyperglycaemia	Any picture, including focal deficits	Capillary glucose first, always
Wernicke encephalopathy	Confusion, ophthalmoplegia, nystagmus, ataxia — often incomplete	High-dose IV thiamine (e.g. 500 mg three times daily) before glucose
PRES	Headache, visual loss, seizures, encephalopathy; hypertension, immunosuppressants, eclampsia	MRI (posterior white-matter oedema); control BP; remove trigger
Sepsis-associated encephalopathy	Fluctuating, symmetrical, often with delirium	Diagnosis of exclusion; treat sepsis
Myxoedema, adrenal crisis	Hypothermia, hyponatraemia, hypotension	TSH, free T4, cortisol; replace hormone

1 TEMPERATURE AS A CONFOUNDER

Core temperature below about 32 °C depresses consciousness, and below about 28 °C may abolish pupillary and brainstem reflexes. After targeted temperature management, sedative clearance is also slowed by cooling. Rewarm and allow for slowed clearance before drawing neurological conclusions.

7

CHAPTER SEVEN

Seizures and status epilepticus

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Suspect non-convulsive seizures and request the right EEG.
- Read an ICU EEG report in ACNS terminology and apply the Salzburg criteria.
- Treat status epilepticus against the clock, and manage refractory status.

71 Non-convulsive seizures — when to suspect, whom to monitor

Non-convulsive seizures produce no motor signs, which is exactly why they are missed. In a landmark series of critically ill patients on continuous EEG, about one in five had seizures and more than 90% of those were purely electrographic.⁵¹ **OBS**

WHEN TO SUSPECT

- Conscious level lower than structural imaging explains.
- Failure to wake as expected after a seizure — a post-ictal state lasting more than 30–60 minutes deserves an EEG.
- Fluctuating consciousness without a new structural cause.
- Subtle signs: eyelid or facial twitching, nystagmoid eye jerks, gaze deviation, automatisms, unexplained autonomic instability.
- After convulsive status that has been "controlled" — electrographic seizures persist in a substantial minority.
- Known risk states: SAH, ICH, TBI, CNS infection, post-cardiac arrest, sepsis with renal failure (cefepime).

WHO NEEDS CONTINUOUS EEG

The ACNS consensus lists indications including:⁵²

CONSENSUS

- Persistent unexplained altered consciousness.
- After convulsive SE, until the patient is clearly waking.
- Patients under neuromuscular blockade or in pharmacological coma.
- Post-cardiac arrest — for seizures and for prognosis.
- Paroxysmal events of uncertain nature.
- Detection of ischaemia after SAH (specialist centres).

1 A SHORT EEG CAN MISLEAD

- A routine 20–30 minute recording misses intermittent seizures. In the same series, the first seizure was captured within 24 hours in most non-comatose patients, but comatose patients often needed 48 hours or more.⁵¹
- If suspicion is high, ask for continuous monitoring rather than accepting a normal short study.

★ HUNT THE CAUSE WHILE YOU TREAT

Glucose, sodium, calcium, magnesium; sepsis; alcohol and drug withdrawal; missed antiseizure doses; drug toxicity (cefepime, carbapenems lowering valproate levels, bupropion, tramadol); new structural lesion; CNS infection; autoimmune or paraneoplastic encephalitis — especially in refractory cases.

7.2 Reading the ICU EEG report

The ACNS 2021 standardised terminology gives every rhythmic and periodic pattern a name built from location (main term 1) and pattern type (main term 2), with modifiers. Knowing the grammar lets you read any report.⁵³ **ACNS 2021**

Main term 1 — where	Main term 2 — what
G generalised	PDs periodic discharges
L lateralised	RDA rhythmic delta activity
BI bilateral	SW spike-and-wave or sharp-and-wave
independent	
UI unilateral	
independent	
Mf multifocal	

Examples: LPDs (lateralised periodic discharges), GPDs, LRDA, GRDA, BIPDs.

Plus modifiers ("F" superimposed fast activity, "R" rhythmic, "S" sharp) increase the association with seizures. SIRPIDs are patterns induced by stimulation.

DEFINITIONS THAT CHANGE MANAGEMENT

Term	ACNS 2021 definition (abbreviated)
Electrographic seizure	Epileptiform discharges averaging > 2.5 Hz for ≥ 10 s, or any pattern with definite evolution lasting ≥ 10 s
Electrographic status epilepticus	Electrographic seizure for ≥ 10 continuous minutes, or for ≥ 20% of any 60-minute period
Electroclinical seizure	EEG pattern with a time-locked clinical correlate, or one that improves clinically and electrographically with an antiseizure drug
Ictal–interictal continuum (IIC)	Patterns that do not meet seizure criteria but may contribute to injury — e.g. PDs or SW at 1–2.5 Hz, or plus-modified patterns. Management is individualised.

SALZBURG CRITERIA FOR NCSE

In patients without a known epileptic encephalopathy, NCSE is diagnosed by any of:⁵⁴

1. Epileptiform discharges > 2.5 Hz; **or**
2. Epileptiform discharges ≤ 2.5 Hz, or rhythmic delta/theta > 0.5 Hz, **plus one of**:
 - EEG *and* clinical improvement after an IV antiseizure drug;
 - subtle clinical ictal phenomena during the pattern;
 - typical spatiotemporal evolution.

EEG improvement without clinical improvement, or fluctuation without evolution, makes NCSE *possible*. In the validation study the criteria had a diagnostic accuracy of about 92%. **OBS**

★ THE ANTISEIZURE DRUG TRIAL

When a pattern sits on the IIC, give a non-sedating IV antiseizure drug (e.g. levetiracetam or lacosamide) — or a small benzodiazepine dose — and look for both EEG resolution and clinical improvement. Both together support NCSE; EEG change alone does not.

I POST-ARREST EEG

After cardiac arrest, suppression and burst-suppression with identical bursts are malignant patterns; continuous normal-voltage background is benign (**p. 54**).⁵⁵

? QUESTIONS TO ASK THE NEUROPHYSIOLOGIST

- Is this a seizure, NCSE, or an ictal–interictal pattern — and by which criteria?
- Is the background continuous, reactive, and how much is explained by sedation?
- Has the pattern changed since the last review, and with which drug?

7.3 Convulsive status epilepticus — the ladder

Status epilepticus is treated against the clock, not against the appearance of the patient. The two commonest errors are under-dosing the benzodiazepine and delaying the second-line drug. The timeline follows the AES 2016 guideline; second-line choices are informed by ESETT.^{56,57} [AES 2016](#)

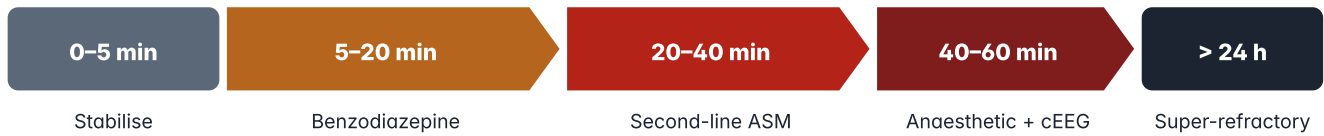


Figure 7.1 Time-based escalation in convulsive status epilepticus. Original schematic.

0–5 min STABILISE

- Airway, oxygen, IV access, glucose (treat if < 60 mg/dL / 3.3 mmol/L — **thiamine 100 mg first** in adults at risk), ECG, bloods including ASM levels and toxicology.

5–20 min BENZODIAZEPINE

- **Lorazepam 0.1 mg/kg IV** (max 4 mg per dose; may repeat once), or **diazepam 0.15–0.2 mg/kg IV** (max 10 mg per dose; may repeat once).
- No IV access: **midazolam 10 mg IM** (> 40 kg) — at least as effective as IV lorazepam prehospital.⁵⁸ [RAMPART](#)
- Give a **full dose** — respiratory depression is more often the seizure than the drug.

20–40 min SECOND LINE

- **Levetiracetam 60 mg/kg** (max 4500 mg) or **fosphenytoin 20 mg PE/kg** (max 1500 mg PE) or **valproate 40 mg/kg** (max 3000 mg).
- ESETT: the three were similarly effective — about half of patients stopped seizing — with similar adverse event rates.⁵⁹ [ESETT](#) Choose on comorbidity: avoid valproate in liver disease, pregnancy and mitochondrial disease; fosphenytoin causes hypotension and arrhythmia.
- **Phenobarbital 15–20 mg/kg** is an alternative when others are unavailable.

40–60 min REFRACTORY

- Intubate and start continuous EEG. Anaesthetic infusion: **midazolam** (0.2 mg/kg bolus, then 0.05–2 mg/kg/h), **propofol** (1–2 mg/kg, then 2–5 mg/kg/h, watch PRIS) or **pentobarbital/thiopental**.
- Titrate to cessation of electrographic seizures or burst-suppression as agreed with neurology; usually maintain for 24–48 h before a slow wean.

! TWO ERRORS TO AVOID

- Small repeated benzodiazepine doses (e.g. 2 mg lorazepam at a time) — give the weight-based dose.
- Waiting to "see if the benzodiazepine works" before preparing the second-line drug — draw it up at the same time.

C CASE IN PRACTICE — THE 2 MG TRAP

A 70 kg man seizing continuously receives lorazepam 2 mg, then 2 mg more ten minutes later, while phenytoin is "being drawn up". At 35 minutes he is still seizing.

Resolution. The correct first dose was 4 mg (0.1 mg/kg, capped), with the second-line drug drawn up at the same time. The delay, not the drugs, made him refractory.

7.4 Refractory status, maintenance and post-anoxic myoclonus

Refractory SE continues despite a benzodiazepine and one adequately dosed second-line drug. Super-refractory SE continues or recurs 24 hours or more after anaesthesia was started, including on weaning.⁵⁷

SUPER-REFRACTORY STATUS

- Add a second non-sedating ASM (e.g. lacosamide, levetiracetam, valproate, perampanel, topiramate) — polytherapy is usual.
- **Ketamine** infusion — NMDA receptor antagonism targets the receptor changes of prolonged SE; haemodynamically favourable.
- **Immunotherapy** early when no cause is found: high-dose methylprednisolone, IVIg or plasma exchange; then second-line agents.
- Pursue the cause: new-onset refractory SE (NORSE) is frequently autoimmune or paraneoplastic.

AFTER THE LOAD — MAINTENANCE

Drug	Maintenance (adult)	Monitoring
Levetiracetam	1000–1500 mg every 12 h	Renal dose adjustment; augmented clearance in young trauma patients; agitation
Valproate	15–45 mg/kg/day divided	Trough 50–100 mg/L; ammonia, LFTs, platelets; carbapenems lower levels sharply
Phenytoin	Adjust to level	Total 10–20 mg/L; free 1–2 mg/L; correct for albumin or measure free level
Lacosamide	100–200 mg every 12 h	PR interval

MYOCLONUS AFTER CARDIAC ARREST

Status myoclonus

Continuous, generalised myoclonus lasting 30 minutes or more within 72 hours of arrest, typically with a malignant EEG background. In this context it is one of the predictors of poor outcome in the ERC/ESICM algorithm — never on its own.⁶⁰

Lance–Adams syndrome

Action myoclonus in a patient who is regaining consciousness, with a continuous or reactive EEG background. It is compatible with good recovery. Record the EEG during the jerks — the background separates the two.

★ TEACHING POINT

Continuous EEG is mandatory once anaesthetic infusions start — you cannot titrate what you cannot see. Weaning without EEG risks unrecognised recurrence.

© CASE IN PRACTICE — NEW-ONSET REFRACTORY STATUS

A healthy 24-year-old develops fever, then seizures refractory to lorazepam, levetiracetam, valproate and midazolam. MRI is normal; CSF shows mild pleocytosis.

Resolution. NORSE. Ketamine plus early steroids and IVIg stopped seizures on day 6; an ovarian teratoma and NMDA receptor antibodies were found later. Immunotherapy before the antibody result shortened the course.

8

CHAPTER EIGHT

Prognosis and communication

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Apply the ERC/ESICM 2025 neuroprognostication algorithm after cardiac arrest.
- Recognise the self-fulfilling prophecy and the confounders that invalidate an assessment.
- Use prognostic models in TBI and ICH appropriately, and communicate uncertainty honestly.

8.1 Principles that protect the patient

Prognostication is the highest-stakes assessment in this book and the one where the discipline of the method matters more than any single finding. Most of the evidence comes from cohorts in which life-sustaining treatment was withdrawn on the basis of the very predictors being studied.^{60,61}

Withdrawal of life-sustaining treatment based on a single early finding creates the poor outcome it predicted.

THE SELF-FULFILLING PROPHECY

If a predictor is used to withdraw treatment, every patient with that finding dies, and the predictor appears perfect. This bias inflates the apparent specificity of almost every prognostic test in brain injury. The defence is procedural:

- Wait — the right interval differs by condition.
- Clear every confounder first.
- Require several concordant predictors from different modalities.
- Document the reasoning.

CONFOUNDERS THAT INVALIDATE AN ASSESSMENT

- Sedatives, opioids, neuromuscular blockers — washout adjusted for organ function and temperature.
- Hypothermia, including recent TTM.
- Severe hypotension or shock.
- Metabolic derangement: glucose, sodium, urea, ammonia, CO₂.
- Seizures and NCSE.
- Sepsis-associated encephalopathy and drug toxicity.

★ THREE QUESTIONS BEFORE ANY PROGNOSTIC STATEMENT

1. Is the examination valid today — are all confounders cleared?
2. Have we waited long enough for this condition?
3. Do at least two independent modalities agree?

If any answer is "no", the outcome is indeterminate — and indeterminate means continue supportive care and reassess, not poor.

WHEN IS AN ASSESSMENT RELIABLE? — A PRACTICAL GUIDE

Condition	Earliest point for a formal prognostic judgement
Cardiac arrest	≥ 72 h after ROSC, after rewarming and sedation washout
Severe TBI	Not in the first days; recovery continues for months — reassess serially
Intracerebral haemorrhage	Full care for at least the first day; avoid early limitation based on scores alone
Aneurysmal SAH	After resuscitation, CSF drainage and aneurysm treatment

8.2 After cardiac arrest — the ERC/ESICM 2025 algorithm

The 2025 guideline keeps the multimodal, two-predictor structure of 2021 and makes two important changes: the algorithm now applies to **all unconscious patients with a motor score of 5 or less** at 72 hours (previously 3 or less), and it presents **indicators of a good outcome** alongside the predictors of a poor one.^{60,62,63} [ERC/ESICM 2025](#)

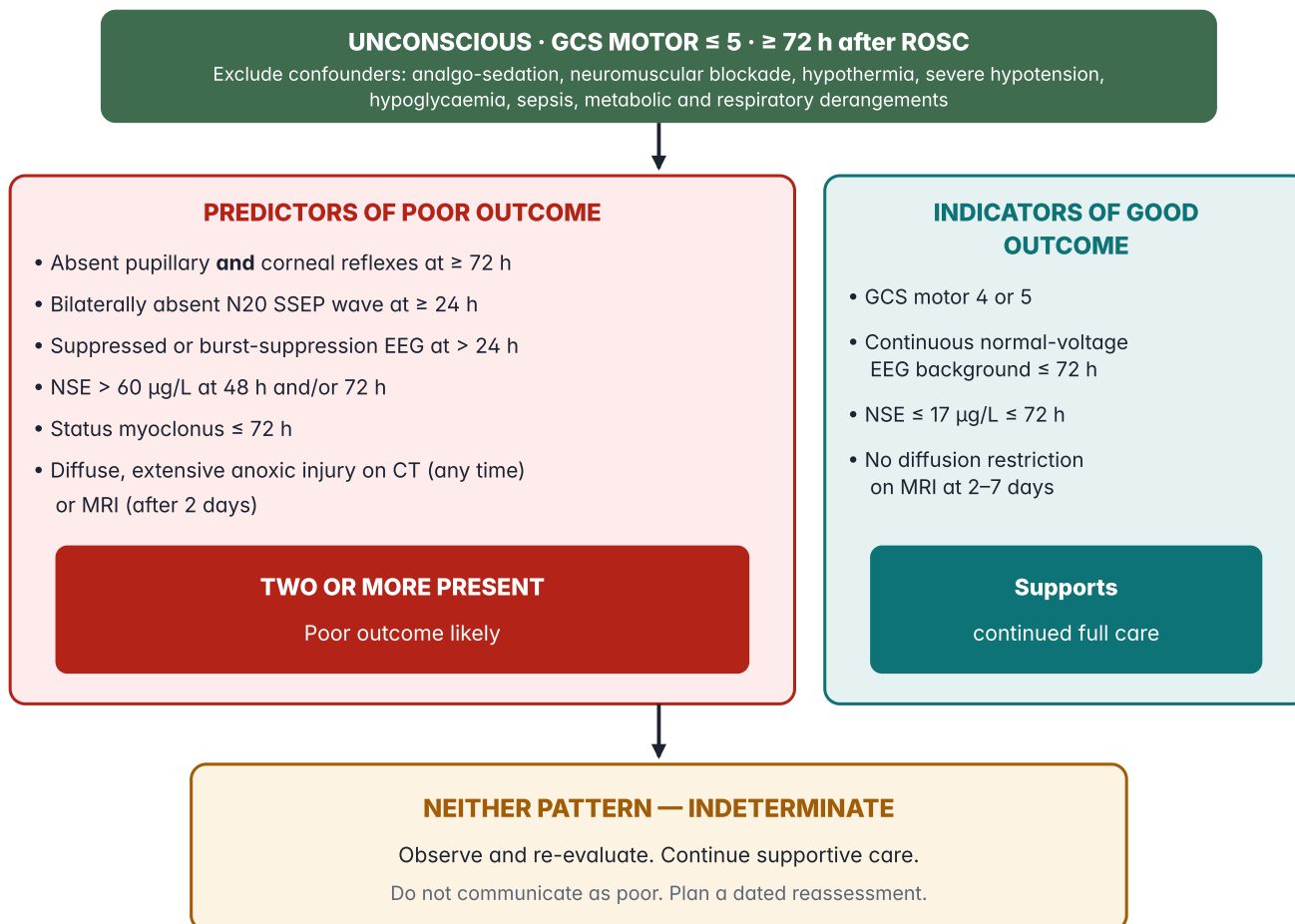


Figure 8.1 Neuroprognostication after cardiac arrest — criteria from ERC/ESICM 2025 (as summarised by Resuscitation Council UK); layout original.

THE INDETERMINATE GROUP IS LARGE

In validation cohorts of the 2021 algorithm a substantial proportion of patients remained indeterminate after full assessment, and some of them recovered well. The 2025 good-outcome indicators were added partly to help this group. Indeterminate is a clinical state with its own plan, not a soft way of saying poor.

BEFORE YOU START

- At least 72 hours after ROSC, and after rewarming and sedation washout — which may be later.
- Brain death has its own criteria ([p. 58](#)).

Day 0–1 ROSC

Treat the cause, prevent fever; early EEG for seizures; SSEP from 24 h.

Day 2–3 BIOMARKERS

NSE at 48 and 72 h (check haemolysis). Begin sedation washout once temperature is controlled.

≥ Day 3 ASSESS

Examination off confounders; MRI day 2–7; multimodal review; family meeting.

8.3 Each modality — strengths and traps

Modality	Finding and timing	Strength	Traps
Pupillary and corneal reflexes	Bilaterally absent at ≥ 72 h	High specificity when confounders are excluded; bedside	Drug suppression; corneal reflex highly susceptible to sedation and to examiner technique. Pupillometry improves objectivity.
Motor response	Not a poor-outcome predictor by itself; M ≤ 5 is the entry criterion; M4–5 is a good-outcome indicator	Simple	Grossly confounded by sedation and blockade
Myoclonus	Status myoclonus ≤ 72 h	Strong when with malignant EEG	Must be distinguished from Lance–Adams; record EEG during jerks
SSEP	Bilaterally absent cortical N20 at ≥ 24 h	Little affected by sedation; very specific	Electrical noise and muscle artefact; needs experienced interpretation; presence of N20 does not predict good outcome
EEG	Suppression or burst-suppression at > 24 h ("highly malignant") ⁵⁵	Widely available; also detects seizures	Sedation causes suppression — interpret with doses; reactivity testing is not standardised
NSE	> 60 $\mu\text{g/L}$ at 48 and/or 72 h; ≤ 17 $\mu\text{g/L}$ suggests good outcome	Objective, cheap, serial trend useful	Haemolysis falsely raises NSE; neuroendocrine tumours; assay variation
Imaging	Diffuse oedema on CT (loss of grey–white differentiation); extensive diffusion restriction on MRI at 2–7 days	Shows extent and distribution	Subjective without quantitative thresholds; early CT may be normal

THREE FRAMEWORKS — WHAT THEY SHARE AND WHERE THEY DIFFER

	ERC/ESICM 2025 ⁶⁰	NCS 2023 ⁶¹	AHA 2025 ⁶⁴
Approach	Algorithm: two or more predictors; good-outcome indicators	GRADE recommendations on individual predictors; explicit statements on reliability	Multimodal approach within post-arrest care guideline
Timing	≥ 72 h after ROSC, confounders excluded	Predictor-specific; most clinical predictors at ≥ 72 h	Delayed, multimodal; consult current text
Shared ground	No single finding determines outcome · clear confounders first · use several modalities · communicate indeterminacy honestly · avoid early withdrawal based on prognosis alone		

I WHICH ONE DO I FOLLOW?

Use the framework your institution has adopted and name it in the notes. Where they differ, the more conservative reading protects the patient.

C CASE IN PRACTICE — THE NSE THAT WAS NOT NEURONAL

At 72 hours NSE is 74 $\mu\text{g/L}$ in a patient with a motor score of 3, intact pupillary and corneal reflexes and a continuous EEG. The sample is haemolysed.

Resolution. Haemolysis falsely raises NSE. With one doubtful predictor and none concordant, the outcome was indeterminate; a clean repeat was 22 $\mu\text{g/L}$ and she followed commands on day 8.

8.4 Prognosis in TBI, stroke and haemorrhage

Outside cardiac arrest there is no single algorithm. Validated models estimate risk in groups; none should be the sole basis for withdrawing care from an individual.

Traumatic brain injury

IMPACT (core: age, GCS motor score, pupillary reactivity; extended: CT characteristics, hypoxia, hypotension; lab: glucose, haemoglobin) predicts 6-month mortality and unfavourable outcome.⁶⁵

CRASH models (basic and CT) include low- and middle-income cohorts and give 14-day mortality and 6-month outcome.⁶⁶

Both are free online calculators. Recovery after severe TBI continues for months to years; many patients thought to have poor prognosis at one month improve substantially by one year.

Intracerebral haemorrhage

The ICH score ([p. 41](#)) and similar scores were derived where early care limitation was common. The AHA 2022 guideline cautions against using them alone to limit care and supports careful early full treatment with reassessment.³⁷

Aneurysmal SAH

Poor admission grade predicts poor outcome, but grade must be reassessed after resuscitation and CSF drainage. A substantial minority of poor-grade patients achieve good outcomes with aggressive care.³³

Ischaemic stroke and DoC

Infarct volume, location, age and pre-stroke function dominate. For prolonged disorders of consciousness, see the recovery timelines and CMD on [p. 13](#).²

TIME-LIMITED TRIALS

When prognosis is uncertain, a time-limited trial of full treatment — with agreed goals, a defined period and explicit criteria for reassessment — respects both the patient's possible recovery and their values. It turns an open-ended "wait and see" into a plan the family can understand.

★ TEACHING POINT

Prognostic models describe what happened to patients like this one in the past, under the care they received. They inform; they do not decide.

● CASE IN PRACTICE — A TIME-LIMITED TRIAL

A 67-year-old has a large left ICH with intraventricular extension; ICH score 3. The family asks whether to continue. The patient had said he would not want to live dependent on others for all care.

Resolution. The team proposes five days of full treatment with an EVD and reassessment on a fixed date. On day 5 he follows simple commands with the left hand but remains aphasic and hemiplegic. With a clear picture rather than a score, the family and team agree goals together — the trial gave both time and information.

8.5 Communicating uncertainty — the family meeting

Families tolerate uncertainty far better than they tolerate surprise. The aim of the meeting is a shared understanding of what is known, what is not yet known, and when you will know more — and of what the patient would want.

BEFORE THE MEETING

- Agree the message within the team — nurses, consultants, neurology, neurosurgery. A family that hears two versions trusts neither.
- Confirm that the examination is valid (confounders cleared) or say explicitly that it is not yet.
- Quiet room, phones off, an interpreter (not a family member) if needed, the bedside nurse present.

DURING THE MEETING

1. **Ask** what they already understand.
2. **Tell** in plain language, in small pieces. Describe function, not scores: "He is not yet able to follow commands" means more than any number.
3. **Name the uncertainty**, the confounders still pending, and the specific date of the next reassessment.
4. **Respond to emotion** before information; allow silence.
5. **Ask about the patient's values**: what would he say about a life with this level of disability? Shift the burden from "what do you want us to do?" to "what would he want?"
6. **Summarise** and agree the next step and the next meeting.

PHRASES THAT HELP

Instead of	Try
"There is nothing more we can do."	"We will always care for him. What we need to decide is which treatments still help him."
"His GCS is 5."	"He opens his eyes to pain but does not yet respond to us."
"The prognosis is poor."	"We are worried he may not wake up. We will know more after the tests on Thursday."
"Do you want everything done?"	"What mattered most to him? How would he feel about...?"

I CULTURAL AND RELIGIOUS CONTEXT

Decision-making, the role of extended family and religious authority, and the legal framework for withdrawing or withholding treatment vary between countries and communities. Follow national regulations and institutional policy, involve a religious adviser when the family wishes, and document who took part and what was agreed.

★ WRITE IT DOWN

Document the examination so the next person can repeat it — stimulus, site, response in each limb, pupils in millimetres, time — and document the meeting: who attended, what was said, what was understood, the decisions and the date of review.

E VALUE — A STRUCTURE WITH EVIDENCE

Value what the family says · Acknowledge emotions · Listen · Understand the patient as a person · Elicit questions. In a randomised trial in French ICUs, a proactive end-of-life conference using this approach with a bereavement leaflet reduced symptoms of post-traumatic stress, anxiety and depression in relatives at 90 days.⁶⁷ RCT

9

CHAPTER NINE

Death by neurological criteria

AFTER THIS CHAPTER YOU SHOULD BE ABLE TO

- Confirm the prerequisites before any examination begins.
- Exclude the mimics of brain death systematically.
- Perform the clinical examination and apnoea test, and know when ancillary testing is needed.

9.1 Concept and prerequisites

Death by neurological criteria (DNC, "brain death") is the complete and permanent loss of brain function: coma, absent brainstem reflexes and apnoea, from a known and irreversible cause. Two international reference documents frame current practice — the World Brain Death Project (2020) and the AAN/AAP/CNS/SCCM consensus guideline (2023).^{68,69} **CONSENSUS**

! NATIONAL LAW COMES FIRST

Criteria, the number of examinations and examiners, required specialties, observation periods and ancillary testing differ between countries. In the Kingdom of Saudi Arabia, determination follows the national criteria and procedures coordinated by the Saudi Center for Organ Transplantation (SCOT) and institutional policy. This chapter describes the internationally shared clinical standard; it does not replace your national protocol.

PREREQUISITES — ALL MUST BE MET BEFORE THE EXAMINATION

Prerequisite	Standard (AAN 2023, adults) ⁶⁹
Established cause	A known, catastrophic, irreversible brain injury consistent with the clinical picture, supported by neuroimaging
Observation after hypoxic–ischaemic injury	At least 24 hours after cardiac arrest or other hypoxic–ischaemic injury before evaluation
Temperature	Core temperature $\geq 36^{\circ}\text{C}$
Blood pressure	SBP ≥ 100 mmHg or MAP ≥ 75 mmHg (vasopressors permitted)
Drugs	No CNS-depressant drug effect — allow adequate clearance (commonly at least five half-lives, longer with organ dysfunction or after hypothermia) or measure levels
Neuromuscular blockade	Excluded — train-of-four with four twitches, or deep tendon reflexes present
Metabolic and endocrine	No severe derangement that could explain or contribute to the picture (sodium, glucose, acid–base, uraemia, hepatic failure, endocrine crisis)

! IF A PREREQUISITE CANNOT BE MET

If a confounder cannot be excluded — for example, drug clearance cannot be established, or the cause is not clear — clinical determination cannot proceed, and an ancillary test is needed where national criteria allow it (p. 61).

9.2 Mimics — conditions that look like brain death

A short list of conditions can reproduce the entire picture — fixed pupils, absent brainstem reflexes, no motor response, even an isoelectric EEG — while remaining fully or partly reversible. Several have been mistaken for brain death in published reports.⁶⁸

Mimic	How it imitates	How it is excluded
Locked-in syndrome	Quadriplegia and anarthria look like absent motor response	Vertical eye movements and blink to command are preserved — test them specifically; MRI shows a ventral pontine lesion
Fulminant Guillain–Barré syndrome	Severe axonal polyneuropathy can extend to the cranial nerves and, rarely, the pupils	History of progressive weakness; consciousness and EEG preserved; nerve conduction studies
Sedative-hypnotics, baclofen	Fixed pupils, absent brainstem reflexes, isoelectric EEG	History, levels, adequate washout — longer in renal failure and after hypothermia
Neuromuscular blockade	Absent motor and brainstem responses	Train-of-four; sugammadex reversal for aminosteroids
Hypothermia	Progressive loss of reflexes and EEG activity with falling core temperature	Rewarm to $\geq 36^{\circ}\text{C}$ before testing
Shock	Reflexes suppressed by poor perfusion	Restore SBP ≥ 100 / MAP ≥ 75 mmHg
Severe metabolic or endocrine disorder	Diffuse suppression (hepatic, uraemic, myxoedema, hypoglycaemia)	Correct; confirm the structural cause is sufficient on its own
Organophosphate and some snake envenomations	Fixed pupils and flaccid paralysis	History; cholinesterase level; time

! DO NOT SHORT-CUT THE SCREEN

A single missed confounder invalidates the whole assessment, however convincing the reflex examination looks. If any item is unresolved, the picture is indeterminate: return to it once corrected. That is a delay, not a failure.

I MOVEMENTS THAT DO NOT EXCLUDE BRAIN DEATH

Spinal reflexes and automatisms — triple flexion, plantar responses, finger jerks, the Lazarus sign, sweating, flushing and tachycardia — can occur after brain death. They arise from the spinal cord and do not exclude the diagnosis, but they must be judged by an experienced examiner.

★ TEACHING POINT

Brain death is a diagnosis of exclusion as much as a set of positive findings. The prerequisites and the mimic screen are one assessment, not two — and both are documented before the first reflex is tested.

C CASE IN PRACTICE — FIXED PUPILS THAT WERE NOT BRAIN DEATH

A 45-year-old on haemodialysis is found comatose with absent pupillary, corneal and oculoccephalic reflexes and no motor response. She had been prescribed baclofen 20 mg three times daily a week earlier. CT is normal.

Resolution. Baclofen accumulates in renal failure and can abolish all brainstem reflexes. With no structural cause on imaging, the prerequisites were not met; after haemodialysis she woke within 48 hours.

9.3 The clinical examination and the apnoea test

The examination demonstrates three things: coma, absence of all brainstem reflexes, and apnoea. Each element is tested deliberately and documented.^{68,69}

1 · COMA

No eye opening and no motor response (other than spinal reflexes) to noxious stimuli applied above and below the foramen magnum — supraorbital pressure, temporomandibular pressure, nail-bed pressure in all limbs.

2 · BRAINSTEM REFLEXES — ALL ABSENT

- **Pupils:** non-reactive to bright light; usually mid-position or dilated. Pupillometry if available.
- **Oculocephalic:** no eye movement on brisk head turning (if the cervical spine is cleared).
- **Oculovestibular:** no eye movement during 1 minute of observation after irrigating each ear with 50 mL of ice water, head at 30°, 5 minutes between ears.
- **Corneal:** no blink to a cotton tip on the cornea.
- **Facial:** no grimace to supraorbital or TMJ pressure.
- **Gag and cough:** no response to pharyngeal stimulation or deep tracheal suction.

AAN 2023 requires one complete examination in adults (two in children); many national criteria require two examinations by different physicians.

3 · APNOEA TEST

Prepare

- Prerequisites met; SBP ≥ 100 / MAP ≥ 75 ; core ≥ 36 °C.
- Pre-oxygenate with FiO₂ 1.0 for at least 10 minutes.
- Baseline arterial gas with PaCO₂ near normal (35–45 mmHg).

Disconnect

- Supply oxygen by tracheal insufflation catheter or CPAP via the ventilator to maintain oxygenation.
- Watch the chest and abdomen continuously for any respiratory effort.

Measure

- Arterial gas after about 8–10 minutes, and as needed until the target is met.

Interpret

- **Positive (consistent with DNC):** no respiratory effort with PaCO₂ ≥ 60 mmHg and ≥ 20 mmHg above baseline.

Abort

- Refractory hypotension, significant desaturation or arrhythmia: reconnect, draw a gas, and plan an ancillary test if the target was not reached.

I CHRONIC CO₂ RETENTION

In patients with chronic hypercapnia the threshold is uncertain; national criteria and expert advice — and often an ancillary test — are needed.

C CASE IN PRACTICE — A SINGLE BREATH

During an apnoea test the bedside nurse sees one shallow abdominal movement at seven minutes. The final PaCO₂ is 68 mmHg, 30 above baseline.

Resolution. Any respiratory effort means the test is *not* consistent with DNC, whatever the gas shows. Determination stopped and was revisited later.

9.4 Ancillary tests, documentation and the donor

Ancillary tests are not a substitute for the clinical examination. They are used when part of the examination or apnoea test cannot be completed or interpreted safely, or when national law requires them.⁶⁹

WHICH TEST

Test	Status in AAN 2023
Four-vessel catheter angiography	Accepted — absent intracranial flow
Radionuclide perfusion scintigraphy	Accepted — absent uptake ("hollow skull")
Transcranial Doppler	Accepted with expertise — reverberating flow or systolic spikes
EEG, SSEP	Not recommended in adults (test cortex or pathways, not whole-brain flow)
CT or MR angiography	Not recommended in AAN 2023; used in some national protocols

The World Brain Death Project likewise prefers tests of blood flow. Check which tests your national criteria recognise.⁶⁸

WHEN AN ANCILLARY TEST IS NEEDED

- Part of the examination cannot be done — facial trauma, ruptured tympanic membranes, high cervical cord injury.
- The apnoea test cannot be completed safely or is inconclusive.
- A confounder cannot be excluded.

DOCUMENTATION

- The cause and the imaging that supports it.
- Each prerequisite, with values and times (temperature, BP, drug levels or timing, TOF).
- Each reflex tested and the result.
- The apnoea test: baseline and final gases, duration, observation of effort.
- Any ancillary test, its indication and result.
- Names and roles of examiners; time of death as defined in local law (commonly the time the determination is completed).

PHYSIOLOGY AFTER BRAIN DEATH — THE POTENTIAL DONOR

Loss of hypothalamic and brainstem control produces predictable problems:

- **Diabetes insipidus** — desmopressin, replace free water.
- **Vasoplegia** — vasopressin, noradrenaline; hormone therapy per local protocol.
- **Hypothermia**, coagulopathy, electrolyte swings.
- The donation conversation is led by the organ procurement team, separately from the determination of death.

★ TEACHING POINT

Speak about death plainly. "Your father has died; his brain has stopped working completely and permanently" is kinder than "brain dead", which families often hear as "almost dead".

1 CONSENT AND THE APNOEA TEST

Whether families must be informed of, or consent to, determination and the apnoea test differs between jurisdictions. Inform the family that testing is planned, explain what it involves, and follow national law and institutional policy. Document the conversation.

A Coma examination — documentation template

Photocopy or print this page for serial examinations. Use the same stimulus and the same words every time.

Patient / ID	Date	Time	Examiner
Sedation running now (drug, dose) and time last stopped		RASS	Temp · MAP · glucose · Na

AROUSAL AND AWARENESS

Eye opening: spontaneous to voice to pressure none	Commands: obeys inconsistent none	Visual fixation / pursuit: yes no
	Look up / down / blink: yes no	Blink to threat: R L
GCS: E ___ V ___ M ___ (NT where untestable) GCS-P ___		FOUR: E ___ M ___ B ___ R ___ = ___ / 16

PUPILS

	Size (mm)	Shape	Direct	Consensual	NPi
Right					
Left					

BRAINSTEM REFLEXES

Reflex	Right	Left	Notes
Corneal			
Eye position at rest			conjugate / deviation / skew / roving / bobbing
Oculocephalic / calorics			C-spine cleared?
Grimace			
Cough (deep suction)			
Gag			

MOTOR — STIMULUS USED:

	Best response (obeys / localises / withdraws / abnormal flexion / extension / none)	Tone	Plantar
Right arm			—
Left arm			—
Right leg			
Left leg			

Breathing: pattern in words; triggering above set rate by ___ /min	Abnormal movements: myoclonus / twitching / asterixis / tremor
Change since last examination, and action taken (CT, senior informed, EEG, sedation change)	

B Drug reference — adult starting doses

Collected from the chapters for quick reference. Every dose is a starting point for a typical adult with normal renal and hepatic function; confirm against weight, organ function, interactions and your formulary.

Drug	Dose	Indication	Key cautions
Raised ICP			
Mannitol 20%	0.5–1 g/kg IV over 15–20 min (up to 1.5 g/kg in herniation)	Raised ICP	Osmolar gap > 20 → withhold; hypovolaemia
Hypertonic saline 3%	250 mL bolus (2–5 mL/kg)	Raised ICP	Sodium every 4–6 h
Hypertonic saline 23.4%	30 mL over 10–20 min, central line only	Herniation	Never peripherally
Status epilepticus			
Lorazepam	0.1 mg/kg IV (max 4 mg/dose), repeat once	First line	Respiratory depression
Diazepam	0.15–0.2 mg/kg IV (max 10 mg/dose), repeat once	First line	As above
Midazolam	10 mg IM (> 40 kg); infusion 0.05–2 mg/kg/h	First line (IM); refractory	Accumulation in renal failure
Levetiracetam	60 mg/kg IV (max 4500 mg); then 1000–1500 mg 12-hourly	Second line	Renal adjustment
Fosphenytoin	20 mg PE/kg IV (max 1500 mg PE)	Second line	Hypotension, arrhythmia; monitor ECG
Valproate	40 mg/kg IV (max 3000 mg)	Second line	Liver disease, pregnancy, mitochondrial disease; carbapenems
Phenobarbital	15–20 mg/kg IV	Second line alternative	Sedation, hypotension
Propofol	1–2 mg/kg, then 2–5 mg/kg/h	Refractory SE, sedation	PRIS above ~4 mg/kg/h for > 48 h
Sedation, analgesia and haemodynamics			
Dexmedetomidine	0.2–1.4 µg/kg/h infusion (no loading dose in the unstable)	Light, rousable sedation	Bradycardia, hypotension; does not treat seizures
Fentanyl	25–200 µg/h infusion; 25–100 µg bolus before handling	Analgesia-first sedation; ICP spikes	Accumulation with prolonged use
Ketamine	1–2 mg/kg IV bolus; infusion for refractory SE by specialist protocol	Induction in hypotension; super-refractory SE	Confounds eye examination
Labetalol	10–20 mg IV over 2 min, repeat; infusion 0.5–2 mg/min	BP control in ICH, SAH, AIS	Bradycardia, bronchospasm
Nicardipine	5 mg/h, increase by 2.5 mg/h every 5–15 min, max 15 mg/h	BP control	Reflex tachycardia; peripheral phlebitis
Clevidipine	1–2 mg/h, double every 90 s initially, usual max 32 mg/h	BP control	Lipid emulsion; egg/soy allergy
Noradrenaline	0.05–0.5 µg/kg/min, titrated to MAP / CPP target	CPP support	Peripheral use short term only per local policy

Continued on the next page.

DRUG REFERENCE — CONTINUED

Drug	Dose	Indication	Key cautions
Haemorrhage and stroke			
4-factor PCC	By INR and weight (warfarin); commonly 50 IU/kg (factor Xa inhibitors)	Anticoagulant reversal	Thrombosis
Vitamin K	10 mg IV	Warfarin reversal	With PCC, not instead
Idarucizumab	5 g IV	Dabigatran reversal	—
Protamine	1 mg per 100 units heparin in the previous 2–3 h	Heparin reversal	Hypotension, anaphylaxis
Nimodipine	60 mg PO/NG every 4 h for 21 days	aSAH	Hypotension → 30 mg every 2 h
Tranexamic acid	1 g over 10 min, then 1 g over 8 h, within 3 h of injury	TBI (mild–moderate)	Not after 3 h
Infection, neuromuscular, metabolic			
Dexamethasone	10 mg IV every 6 h for 4 days	Bacterial meningitis	Start with first antibiotic dose
Ceftriaxone	2 g IV every 12 h	Bacterial meningitis	Add vancomycin and/or amoxicillin as indicated
Aciclovir	10 mg/kg IV every 8 h	Encephalitis	Renal adjustment; hydrate
IVIg	0.4 g/kg/day for 5 days (2 g/kg total)	GBS, myasthenic crisis	Thrombosis, renal injury, IgA deficiency
Thiamine	500 mg IV three times daily (Wernicke); 100 mg before glucose	Wernicke, malnutrition	Give before glucose
3% saline (hyponatraemia)	150 mL over 20 min, up to three times	Severe symptomatic hyponatraemia	Rise ≤ 10 mmol/L in 24 h
Desmopressin	1–2 µg IV/SC	Central diabetes insipidus	Hyponatraemia; monitor Na
Amantadine	100–200 mg twice daily	Traumatic DoC (weeks 4–16)	Seizure threshold; renal
Airway and neuromuscular			
Rocuronium	1–1.2 mg/kg IV for rapid sequence induction	Intubation; preferred over suxamethonium in GBS, denervation, prolonged immobility	Reduce dose in myasthenia
Sugammadex	2–16 mg/kg IV depending on depth of block	Reversal of rocuronium / vecuronium	Confirm reversal with train-of-four before neurological testing
Plasma exchange	Typically 5 exchanges over 7–14 days	GBS, myasthenic crisis, autoimmune encephalitis	Line complications, hypotension, coagulopathy

1 BEFORE YOU GIVE ANY DOSE

- Weight (actual, ideal or adjusted — know which the drug uses), renal and hepatic function, age, pregnancy.
- Interactions — especially carbapenems with valproate, enzyme inducers with other ASMs, and QT-prolonging combinations.
- Local formulary and protocol take precedence over this table.

C Bedside cards

Three cards for the bedside or the pocket. Each is complete on its own.

60-second coma examination

1. **Glucose.** Airway, SpO₂, MAP.
2. **Arousal:** eyes to voice, to pressure.
3. **Awareness:** command; look up, look down, blink twice.
4. **Pupils:** mm, symmetry, reaction.
5. **Eyes:** position, deviation, doll's eyes.
6. **Corneals, cough, gag.**
7. **Motor:** trapezius pinch — each limb.
8. **Breathing** pattern / triggering.
9. **Drug chart:** what, how much, since when.

Asymmetry → CT now.

Symmetry + reactive pupils → metabolic screen, EEG.

Blown pupil drill

1. Call neurosurgery, senior, CT — together.
2. Airway; avoid hypoxia and hypotension.
3. Head 30°, neck midline, loosen ties.
4. PaCO₂ 30–35 mmHg briefly.
5. 23.4% NaCl 30 mL central *or* 3% 250 mL *or* mannitol 1 g/kg.
6. Sedate, treat seizures.
7. Reverse anticoagulation.
8. CT → theatre / EVD / craniectomy.

Re-check pupils every 5–10 min.

Osmotherapy without a surgical plan is delay.

Status epilepticus

0–5 min ABC, glucose, thiamine.

5–20 min lorazepam 0.1 mg/kg (max 4 mg) *or* midazolam 10 mg IM.

20–40 min levetiracetam 60 mg/kg *or* fosphenytoin 20 mg PE/kg *or* valproate 40 mg/kg.

40–60 min intubate, cEEG, midazolam / propofol / barbiturate infusion.

> 24 h ketamine, immunotherapy, find the cause.

Full doses. Prepare the next drug while giving this one.

Before any prognostic statement

- Confounders cleared: drugs, NMB, temperature, BP, glucose, sodium, CO₂, seizures.
- Waited long enough — ≥ 72 h after cardiac arrest.
- Two or more concordant modalities.
- Indeterminate = continue care, reassess on a stated date.

Localisation in one line each

- **Pupils, vertical gaze** → midbrain.
- **Corneals, horizontal gaze** → pons.
- **Gag, cough, breathing** → medulla.
- **Eyes away from hemiparesis** → hemisphere; **toward** it → pons, seizure, thalamus.
- **Bilateral VI** → pressure, not pons.

Sodium — safe limits

- Severe symptoms: 3% NaCl 150 mL over 20 min, up to ×3, aim +5 mmol/L.
- Max rise 10 mmol/L first 24 h, 8 per day after.
- After SAH: **never fluid-restrict.**
- Polyuria + rising Na + dilute urine → DI: desmopressin.

DNC prerequisites

- Known irreversible cause + imaging.
- ≥ 24 h after hypoxic–ischaemic injury.
- Core ≥ 36 °C; SBP ≥ 100 / MAP ≥ 75.
- No drug effect; TOF 4/4.
- No severe metabolic disorder.
- Follow **national criteria.**

Not waking off sedation

- Accumulation: renal, hepatic, obesity, cold.
- NCSE → continuous EEG.
- New lesion → CT.
- Na, glucose, NH₃, CO₂, urea.
- Residual block → train-of-four.
- Cefepime, baclofen, lithium, valproate.

D Self-assessment — fourteen questions

Single best answer. Answers and explanations follow on the next page.

1. A ventilated patient opens her eyes spontaneously, looks up when asked and blinks twice to command, but has no limb movement to any stimulus. The best description is:

- A. Unresponsive wakefulness syndrome
- B. Locked-in syndrome
- C. Minimally conscious state minus
- D. Coma
- E. Akinetic mutism

2. A patient with a right frontal haematoma has a dilated, unreactive right pupil and a right hemiparesis. The most likely explanation of the hemiparesis is:

- A. A second, left-sided lesion
- B. Kernohan's notch phenomenon
- C. Weber syndrome from a primary midbrain infarct
- D. Todd paresis
- E. Spinal cord injury

3. Before a repeat dose of mannitol, the measured osmolality is 318 and the calculated osmolality 290 mOsm/kg. The best action is:

- A. Give the dose — osmolality is below 320
- B. Give double the dose
- C. Withhold mannitol — the osmolar gap exceeds 20
- D. Switch to continuous mannitol infusion
- E. Give furosemide

4. In the SIBICC algorithm, mild hypocapnia to PaCO₂ 32–35 mmHg belongs to:

- A. Tier 0
- B. Tier 1
- C. Tier 2
- D. Tier 3
- E. It is not recommended

5. A comatose patient on cEEG shows lateralised periodic discharges at 1.5 Hz. After IV levetiracetam the discharges resolve and he begins to localise. This most strongly supports:

- A. An interictal pattern only
- B. Non-convulsive status epilepticus (Salzburg)
- C. Post-anoxic burst-suppression
- D. Sedation effect
- E. Metabolic triphasic waves

11. A patient with severe TBI has ICP 26 mmHg despite Tier 1 measures. Which is a Tier 2 measure in SIBICC?

- A. Pentobarbital coma
- B. Neuromuscular blockade trial
- C. Secondary decompressive craniectomy
- D. Hypothermia to 33 °C
- E. Methylprednisolone

12. Which finding favours a toxic-metabolic over a structural cause of coma?

- A. Unilateral fixed dilated pupil
- B. Skew deviation
- C. Reactive pupils with absent oculocephalic responses and multifocal myoclonus
- D. Conjugate gaze deviation with hemiparesis
- E. Absent corneal reflex on one side

6. Seventy-two hours after cardiac arrest, off sedation and normothermic, a patient has a motor score of 4, a continuous normal-voltage EEG and NSE of 14 µg/L. Under ERC/ESICM 2025:

- A. Poor outcome is likely
- B. Indicators of good outcome are present
- C. The patient is outside the algorithm
- D. Withdrawal can be discussed
- E. SSEP is mandatory before any statement

7. Status epilepticus has continued for 25 minutes after 4 mg of lorazepam. The next step is:

- A. A further 4 mg of lorazepam and wait 20 minutes
- B. Levetiracetam 60 mg/kg, fosphenytoin 20 mg PE/kg or valproate 40 mg/kg
- C. Immediate ketamine
- D. Ketogenic diet
- E. Await the EEG

8. On day 6 after aneurysmal SAH (aneurysm coiled), sodium is 128 mmol/L, urine output is high and fluid balance is negative. The best management is:

- A. Fluid restriction to 1 L/day
- B. Isotonic or hypertonic saline; consider fludrocortisone
- C. Demeclocycline
- D. Tolvaptan
- E. No treatment until below 125

9. Which finding does *not* exclude death by neurological criteria?

- A. Pupils reactive to light
- B. Triple flexion of the legs to nail-bed pressure
- C. Cough to deep tracheal suction
- D. Respiratory effort during the apnoea test
- E. Eye movement on cold caloric

10. A patient with GBS has VC 18 mL/kg, NIF −24 cmH₂O, weak cough and pooled secretions. PaCO₂ is 40 mmHg. The best action is:

- A. Repeat measurements in 6 hours
- B. Start BiPAP
- C. Elective intubation now
- D. Await hypercapnia
- E. Give pyridostigmine

13. For warfarin-associated ICH with INR 3.1, the best reversal is:

- A. Fresh frozen plasma alone
- B. Vitamin K alone
- C. 4-factor PCC plus IV vitamin K
- D. Platelet transfusion
- E. Idarucizumab

14. During an apnoea test, which result is consistent with death by neurological criteria (AAN 2023)?

- A. PaCO₂ 52 mmHg, no effort
- B. PaCO₂ 64 mmHg, 24 above baseline, no effort
- C. PaCO₂ 66 mmHg, one gasp at 6 minutes
- D. PaCO₂ 58 mmHg, 20 above baseline, no effort
- E. SpO₂ falls to 80%, test aborted

ANSWERS AND EXPLANATIONS

1 — B. Vertical eye movements and blink to command show preserved awareness with near-total loss of motor output: locked-in syndrome, usually from ventral pontine infarction. FOUR E4 with M0 is the numerical signature (p. 17).

2 — B. The opposite cerebral peduncle is compressed against the tentorium, producing hemiparesis on the same side as the mass. The pupil remains the reliable sign of the side of the lesion (p. 26).

3 — C. The gap is 28 mOsm/kg, indicating unexcreted mannitol. Withhold the dose; consider hypertonic saline if further osmotherapy is needed (p. 36).

4 — C. Tier 1 uses PaCO₂ at the low end of normal (35–38 mmHg); mild hypocapnia (32–35) is Tier 2 (p. 34).

5 — B. Discharges at ≤ 2.5 Hz plus EEG and clinical improvement after an IV antiseizure drug meet the Salzburg criteria for NCSE (p. 50).

6 — B. Motor 4–5, a continuous normal-voltage EEG within 72 h and NSE ≤ 17 µg/L are the 2025 indicators of good outcome. The patient is inside the algorithm because the motor score is ≤ 5 (p. 54).

7 — B. After an adequate benzodiazepine, go straight to a second-line drug; ESETT found the three similar. Further benzodiazepine boluses delay effective therapy (p. 51).

8 — B. A negative balance with high urine output suggests cerebral salt wasting. Fluid restriction after SAH increases the risk of DCI (p. 45).

9 — B. Spinal reflexes such as triple flexion can persist after brain death. Every other finding shows surviving brainstem function (p. 59).

10 — C. VC below 20 mL/kg, NIF weaker than −30 cmH₂O and bulbar weakness with secretions mean imminent failure. Gas exchange is normal until late; BiPAP is unsafe with bulbar weakness (p. 44).

11 — B. Tier 2 includes mild hypocapnia, a neuromuscular blockade trial and MAP challenge. Barbiturates, craniectomy and mild hypothermia are Tier 3; deeper hypothermia and steroids are not recommended (p. 34).

12 — C. Reactive pupils despite loss of other brainstem responses, with multifocal myoclonus, point to a toxic–metabolic process (p. 15).

13 — C. 4-factor PCC corrects the INR within minutes; vitamin K sustains it. Plasma is slower and needs large volumes (p. 41).

14 — B. The target is PaCO₂ ≥ 60 mmHg and ≥ 20 mmHg above baseline with no respiratory effort; any breath excludes DNC; an aborted test needs an ancillary study (p. 60).

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CHANGELOG

Version	Date	Changes
1.0	October 2026	First public edition.
1.1	October 2026	Adds a 100-question bank with answers and explanations; author photograph.

R References

One numbered list, in order of first citation (Vancouver style). Superscript numbers in the text point here. Guideline editions were checked against the primary record as of October 2026.

1. Posner JB, Saper CB, Schiff ND, Claassen J. *Plum and Posner's Diagnosis and Treatment of Stupor and Coma*. 5th ed. New York: Oxford University Press; 2019.
2. Giacino JT, Katz DI, Schiff ND, et al. Practice guideline update recommendations summary: disorders of consciousness. *Neurology*. 2018;91(10):450–460.
3. Edlow BL, Takahashi E, Wu O, et al. Neuroanatomic connectivity of the human ascending arousal system critical to consciousness and its disorders. *J Neuropathol Exp Neurol*. 2012;71(6):531–546.
4. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale–Revised: measurement characteristics and diagnostic utility. *Arch Phys Med Rehabil*. 2004;85(12):2020–2029.
5. Bodien YG, Allanson J, Cardone P, et al. Cognitive motor dissociation in disorders of consciousness. *N Engl J Med*. 2024;391(7):598–608.
6. Wijdicks EFM. The bare essentials: coma. *Pract Neurol*. 2010;10(1):51–60.
7. Teasdale G, Maas A, Lecky F, et al. The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet Neurol*. 2014;13(8):844–854.
8. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. *Lancet*. 1974;2(7872):81–84.
9. Brennan PM, Murray GD, Teasdale GM. Simplifying the use of prognostic information in traumatic brain injury. Part 1: the GCS–Pupils score. *J Neurosurg*. 2018;128(6):1612–1620.
10. Wijdicks EFM, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. *Ann Neurol*. 2005;58(4):585–593.
11. Oddo M, Taccone FS, Petrosino M, et al. The Neurological Pupil index for outcome prognostication in people with acute brain injury (ORANGE): a prospective, observational, multicentre cohort study. *Lancet Neurol*. 2023;22(10):925–933.
12. Medical Research Council. *Aids to the Examination of the Peripheral Nervous System*. Memorandum no. 45. London: HMSO; 1976.
13. Benganem S, Mazeraud A, Azabou E, et al. Brainstem dysfunction in critically ill patients. *Crit Care*. 2020;24(1):5.
14. Kernohan JW, Woltman HW. Incisura of the crus due to contralateral brain tumor. *Arch Neurol Psychiatry*. 1929;21(2):274–287.
15. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.
16. Baguley IJ, Perkes IE, Fernandez-Ortega JF, et al. Paroxysmal sympathetic hyperactivity after acquired brain injury: consensus on conceptual definition, nomenclature, and diagnostic criteria. *J Neurotrauma*. 2014;31(17):1515–1520.
17. Czosnyka M, Pickard JD. Monitoring and interpretation of intracranial pressure. *J Neurol Neurosurg Psychiatry*. 2004;75(6):813–821.
18. Steiner LA, Czosnyka M, Piechnik SK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. *Crit Care Med*. 2002;30(4):733–738.
19. Le Roux P, Menon DK, Citerio G, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care. *Neurocrit Care*. 2014;21(Suppl 2):S1–S26.
20. Chesnut RM, Temkin N, Carney N, et al. A trial of intracranial-pressure monitoring in traumatic brain injury (BEST:TRIP). *N Engl J Med*. 2012;367(26):2471–2481.
21. Chesnut R, Aguilera S, Buki A, et al. A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med*. 2020;46(5):919–929.
22. Lundberg N. Continuous recording and control of ventricular fluid pressure in neurosurgical practice. *Acta Psychiatr Scand Suppl*. 1960;36(149):1–193.
23. Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. *Intensive Care Med*. 2018;44(8):1284–1294.
24. Hawryluk GWJ, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med*. 2019;45(12):1783–1794.
25. Cook AM, Morgan Jones G, Hawryluk GWJ, et al. Guidelines for the acute treatment of cerebral edema in neurocritical care patients. *Neurocrit Care*. 2020;32(3):647–666.
26. Roberts I, Yates D, Sandercock P, et al. Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial. *Lancet*. 2004;364(9442):1321–1328.
27. Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493–1502.
28. Hutchinson PJ, Koliass AG, Timofeev IS, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med*. 2016;375(12):1119–1130.
29. Hawryluk GWJ, Rubiano AM, Totten AM, et al. Guidelines for the management of severe traumatic brain injury: 2020 update of the decompressive craniectomy recommendations. *Neurosurgery*. 2020;87(3):427–434.
30. Andrews PJD, Sinclair HL, Rodriguez A, et al. Hypothermia for intracranial hypertension after traumatic brain injury. *N Engl J Med*. 2015;373(25):2403–2412.
31. CRASH-3 trial collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. *Lancet*. 2019;394(10210):1713–1723.
32. Marshall LF, Marshall SB, Klauber MR, et al. A new classification of head injury based on computerized tomography. *J Neurosurg*. 1991;75(Suppl):S14–S20.
33. Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the management of patients with aneurysmal subarachnoid hemorrhage: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2023;54(7):e314–e370.
34. Teasdale GM, Drake CG, Hunt W, et al. A universal subarachnoid hemorrhage scale: report of a committee of the World Federation of Neurosurgical Societies. *J Neurol Neurosurg Psychiatry*. 1988;51(11):1457.
35. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28(1):14–20.
36. Frontera JA, Claassen J, Schmidt JM, et al. Prediction of symptomatic vasospasm after subarachnoid hemorrhage: the modified Fisher scale. *Neurosurgery*. 2006;59(1):21–27.

REFERENCES — CONTINUED

37. Greenberg SM, Ziai WC, Cordonnier C, et al. 2022 Guideline for the management of patients with spontaneous intracerebral hemorrhage: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2022;53(7):e282–e361.
38. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001;32(4):891–897.
39. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines. *Stroke*. 2019;50(12):e344–e418.
40. Tao C, Nogueira RG, Zhu Y, et al. Trial of endovascular treatment of acute basilar-artery occlusion (ATTENTION). *N Engl J Med*. 2022;387(15):1361–1372.
41. Jovin TG, Li C, Wu L, et al. Trial of thrombectomy 6 to 24 hours after stroke due to basilar-artery occlusion (BAOCHE). *N Engl J Med*. 2022;387(15):1373–1384.
42. Vahedi K, Hofmeijer J, Juettler E, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol*. 2007;6(3):215–222.
43. van de Beek D, Cabellos C, Dzupova O, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. *Clin Microbiol Infect*. 2016;22(Suppl 3):S37–S62.
44. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol*. 2016;15(4):391–404.
45. van Doorn PA, Van den Bergh PYK, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of Guillain-Barré syndrome. *Eur J Neurol*. 2023;30(12):3646–3674.
46. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. *Neurology*. 2016;87(4):419–425.
47. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Eur J Endocrinol*. 2014;170(3):G1–G47.
48. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU (PADIS). *Crit Care Med*. 2018;46(9):e825–e873.
49. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med*. 2002;166(10):1338–1344.
50. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the Confusion Assessment Method for the ICU (CAM-ICU). *JAMA*. 2001;286(21):2703–2710.
51. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology*. 2004;62(10):1743–1748.
52. Herman ST, Abend NS, Bleck TP, et al. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. *J Clin Neurophysiol*. 2015;32(2):87–95.
53. Hirsch LJ, Fong MWK, Leitinger M, et al. American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol*. 2021;38(1):1–29.
54. Leitinger M, Trinka E, Gardella E, et al. Diagnostic accuracy of the Salzburg EEG criteria for non-convulsive status epilepticus: a retrospective study. *Lancet Neurol*. 2016;15(10):1054–1062.
55. Westhall E, Rossetti AO, van Rootselaar AF, et al. Standardized EEG interpretation accurately predicts prognosis after cardiac arrest. *Neurology*. 2016;86(16):1482–1490.
56. Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults. Report of the Guideline Committee of the American Epilepsy Society. *Epilepsy Curr*. 2016;16(1):48–61.
57. Brophy GM, Bell R, Claassen J, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care*. 2012;17(1):3–23.
58. Silbergleit R, Durkalski V, Lowenstein D, et al. Intramuscular versus intravenous therapy for prehospital status epilepticus (RAMPART). *N Engl J Med*. 2012;366(7):591–600.
59. Kapur J, Elm J, Chamberlain JM, et al. Randomized trial of three anticonvulsant medications for status epilepticus (ESETT). *N Engl J Med*. 2019;381(22):2103–2113.
60. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2025: post-resuscitation care. *Intensive Care Med*. 2025;51(12):2213–2288. doi:10.1007/s00134-025-08117-3
61. Rajasee V, Muehlschlegel S, Wartenberg KE, et al. Guidelines for neuroprognostication in comatose adult survivors of cardiac arrest. *Neurocrit Care*. 2023;38(3):533–563.
62. Resuscitation Council UK. Adult neuroprognostication algorithm 2025 (based on ERC/ESICM 2025). London: Resuscitation Council UK; 2025.
63. Nolan JP, Sandroni C, Böttiger BW, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. *Intensive Care Med*. 2021;47(4):369–421.
64. Hirsch KG, Amorim E, Coppler PJ, et al. Part 11: post-cardiac arrest care: 2025 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2025. doi:10.1161/CIR.0000000000001375
65. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. *PLoS Med*. 2008;5(8):e165.
66. MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. *BMJ*. 2008;336(7641):425–429.
67. Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med*. 2007;356(5):469–478.
68. Greer DM, Shemie SD, Lewis A, et al. Determination of brain death/death by neurologic criteria: the World Brain Death Project. *JAMA*. 2020;324(11):1078–1097.
69. Greer DM, Kirschen MP, Lewis A, et al. Pediatric and adult brain death/death by neurologic criteria determination: consensus guideline. *Neurology*. 2023;101(24):1112–1132.

I Index

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Q Question bank — one hundred questions

Single best answer. One hundred questions written from the nine chapters, in chapter order. Answers, explanations and the page to revisit follow the questions.

HOW TO USE IT

Answer a whole chapter block before checking. Mark the ones you guessed, not just the ones you missed.

WHAT IT TESTS

Bedside decisions, thresholds and doses that the guide ties to a numbered reference.

WHEN YOU MISS ONE

Go to the page given with the answer and reread the red and star boxes there.

1 CONSCIOUSNESS

1. A single small lesion abolishes arousal and produces coma. Where must it lie?

- A. Upper brainstem tegmentum or both thalami
- B. Lower pons, below the level of the trigeminal nuclei
- C. One cerebral hemisphere, if the infarct is large enough
- D. Ventral medulla, at the level of the pyramids
- E. Cerebellar vermis and roof of the fourth ventricle

2. Six weeks after a hypoxic injury a patient has eyes open, sleep–wake cycles and reproducible visual pursuit of a mirror, but no command following. The best classification is:

- A. Emerged from the minimally conscious state
- B. Minimally conscious state plus (MCS+)
- C. Minimally conscious state minus (MCS–)
- D. Unresponsive wakefulness syndrome
- E. Cognitive motor dissociation

3. Which behaviour, shown reliably and consistently, marks emergence from the minimally conscious state?

- A. Intelligible single words
- B. Sustained visual pursuit
- C. Localisation to a noxious stimulus
- D. Functional use of two different objects
- E. Reproducible movement to command

4. On the Coma Recovery Scale–Revised, what determines the diagnosis (UWS, MCS or emergence)?

- A. The highest item reached on each subscale
- B. The mean of the arousal and motor subscales
- C. A total score of 10 or more
- D. The auditory subscale score alone
- E. A total score of 15 or more

5. In the largest multinational study of covert consciousness, roughly what proportion of patients with no observable command following showed command-specific brain activity on task-based fMRI or EEG?

- A. About one in four
- B. About one in ten
- C. About three in four
- D. About one in two
- E. About one in fifty

6. Amantadine to hasten functional recovery after traumatic disorders of consciousness is recommended at which dose and window?

- A. 100 mg once daily, from day 1 after injury
- B. 200 mg twice daily, only after 12 months
- C. 400 mg once daily, from the third month onwards
- D. 50 mg three times daily, weeks 1–4 after injury
- E. 100–200 mg twice daily, weeks 4–16 after injury

7. Dexmedetomidine produces sedation from which the patient can still be roused. Its principal site of action is the:

- A. Ventral tegmental area (dopamine)
- B. Locus coeruleus (noradrenaline, α_2 receptors)
- C. Pedunculopontine nucleus (acetylcholine)
- D. Lateral hypothalamus (orexin)
- E. Tuberomammillary nucleus (histamine)

8. A 61-year-old is found unrousable with small, sluggish pupils, a vertical gaze palsy and symmetrical limb movements. The first CT is normal. The most likely diagnosis is:

- A. Right uncal herniation from a subdural
- B. Lateral medullary (Wallenberg) infarction
- C. Artery of Percheron infarction (both thalami)
- D. Central pontine myelinolysis after correction
- E. Opioid overdose with hypoventilation

9. A 74-year-old with chronic kidney disease is unresponsive 36 hours after laparotomy, on cefepime and a morphine PCA, with small reactive pupils and multifocal myoclonus. CT is unchanged. The best explanation is:

- A. Wernicke encephalopathy from malnutrition
- B. Basilar artery occlusion with pontine infarction
- C. NCSE from a new cortical infarct
- D. Post-operative fat embolism syndrome
- E. Cefepime toxicity plus morphine metabolite build-up

2 BEDSIDE EXAMINATION

10. An intubated patient opens his eyes to pressure and flexes abnormally. How should the GCS be recorded?

- A. GCS 3T
- B. E2 VT M3
- C. GCS 6T
- D. E2 V1 M3 = 6
- E. GCS 5

11. A patient has a GCS of 6 with one pupil unreactive to light. What is the GCS-P?

- A. 3
- B. 4
- C. 5
- D. 6
- E. 7

12. Which GCS component carries most of the prognostic information and should never be buried in a total?

- A. The summed total
- B. Eye opening plus verbal response
- C. Eye opening
- D. Verbal response
- E. Motor response

13. Which change in the GCS counts as deterioration, prompting a pupil check, a senior review and repeat imaging?

- A. A fall of 1 point in the verbal score
- B. A fall to a total of 8 or less, whatever the trend
- C. A fall of 1 point in the total
- D. A fall of 1 point in eye opening
- E. A fall of 1 point in the motor score

14. On the FOUR score, a ventilated patient who triggers breaths above the set ventilator rate scores:

- A. R0
- B. R1
- C. R2
- D. R3
- E. R4

15. On the FOUR score brainstem (B) component, one pupil wide and fixed with corneal reflexes present scores:

- A. B0
- B. B1
- C. B2
- D. B3
- E. B4

16. A FOUR score of 0 means:

- A. Locked-in syndrome must be present
- B. Death by neurological criteria is established
- C. The patient is in unresponsive wakefulness
- D. Treatment can be withdrawn on this basis
- E. A prompt to consider brain death testing only

17. In the swinging light test, both pupils dilate each time the light reaches the left eye. The lesion is in the:

- A. Left sympathetic chain
- B. Right optic nerve
- C. Right oculomotor nerve
- D. Left oculomotor nerve
- E. Left optic nerve

18. Pupils that stay reactive in deep coma usually point to a toxic-metabolic cause. Which of these can abolish the light reflex without structural injury?

- A. Sepsis-associated encephalopathy
- B. Hyponatraemia
- C. Hepatic encephalopathy
- D. High-dose barbiturates
- E. Uraemia

19. Automated pupillometry shows NPi 4.1 on the right and 3.2 on the left. The correct interpretation is:

- A. Abnormal — interocular difference ≥ 0.7
- B. Normal — NPi matters only below 2
- C. Abnormal — the left eye is non-reactive
- D. Normal — both values are 3 or above
- E. Uninterpretable without a pupil gauge

20. A ventilated patient develops a 7 mm unreactive left pupil an hour after an ipratropium nebuliser. CT is unchanged. One drop of 1% pilocarpine fails to constrict it. This indicates:

- A. Left Adie tonic pupil
- B. Left Horner syndrome
- C. Compression of the left oculomotor nerve
- D. Pharmacological blockade of the iris
- E. Left relative afferent pupillary defect

21. Slow, stereotyped flexion of the arm with wrist flexion and thumb adduction to a central stimulus suggests a lesion:

- A. Above the midbrain (hemispheres or diencephalon)
- B. In the cerebellar hemisphere
- C. In the lower medulla, below the vagal nuclei
- D. In the cervical spinal cord
- E. In the peripheral nerves of the arm

22. Which stimulus is needed to distinguish localising from flexion?

- A. A loud voice close to the ear
- B. Plantar stimulation of the sole
- C. Pinprick on the forearm
- D. Supraorbital or trapezius pressure
- E. Nail-bed pressure on each limb

23. A comatose patient has prolonged inspiratory pauses (an inspiratory "cramp"). This apneustic breathing localises to the:

- A. Diencephalon
- B. Bilateral hemispheres
- C. Mid-lower pons
- D. Lower medulla
- E. Cervical cord

3 BRAINSTEM AND LOCALISATION

24. The corneal reflex tests which pathway and level?

- A. II afferent → III efferent, midbrain
- B. V₁ afferent → VII efferent, pons
- C. V₁ afferent → III efferent, midbrain
- D. VIII afferent → III and VI efferent, medulla
- E. IX afferent → X efferent, medulla

25. In an intubated patient, which is the more reliable test of medullary function?

- A. Grimace to supraorbital pressure
- B. Cough to deep tracheal suction
- C. Gag to movement of the tube
- D. Corneal reflex
- E. Oculocephalic reflex

26. Cold water in the right ear of a comatose patient produces tonic conjugate deviation of both eyes to the right, with no fast phase. This means:

- A. Intact brainstem gaze pathways, no cortical correction
- B. Psychogenic unresponsiveness with an intact cortex
- C. A right medial longitudinal fasciculus lesion
- D. A right oculomotor palsy at the tentorium
- E. Severe pontomesencephalic dysfunction

27. An apparently unresponsive patient develops nystagmus with the fast phase away from the irrigated ear during cold calorics. The most likely explanation is:

- A. Vestibulotoxic (aminoglycoside) drug effect
- B. Working cortex — consider psychogenic coma
- C. Deep sedation with a propofol infusion
- D. Bilateral internuclear ophthalmoplegia
- E. Pontine haemorrhage involving the PPRF

28. A comatose patient's eyes are conjugately deviated toward the hemiparetic side. Which lesion fits best?

- A. A large frontal infarct on the side opposite the hemiparesis
- B. An occipital infarct on the side opposite the hemiparesis
- C. A cerebellar infarct on the side of the hemiparesis
- D. A pontine lesion on the side opposite the hemiparesis
- E. A frontal infarct on the same side as the hemiparesis

29. Fast downward jerks of both eyes with a slow return to mid-position are classically seen with:

- A. Extensive pontine lesions
- B. Toxic-metabolic coma with an intact brainstem
- C. Lateral medullary infarction
- D. Dorsal midbrain compression
- E. Bilateral hemispheric dysfunction

30. Which finding is NOT part of the lateral medullary (Wallenberg) syndrome?

- A. Dysphagia and hoarseness
- B. Contralateral hemiparesis
- C. Ipsilateral facial pain and temperature loss
- D. Ipsilateral Horner syndrome
- E. Contralateral body pain and temperature loss

31. The tongue deviates to the left on protrusion with left-sided wasting and fasciculation. The lesion is:

- A. Right corticobulbar tract, above the medulla
- B. Left hypoglossal nerve or nucleus (lower motor neuron)
- C. Left facial nerve
- D. Left corticobulbar tract, above the medulla
- E. Right hypoglossal nerve or nucleus (lower motor neuron)

32. A patient with raised intracranial pressure develops bilateral abducens palsies and no other brainstem signs. This most likely represents:

- A. Bilateral cavernous sinus thrombosis
- B. Wernicke encephalopathy
- C. A focal pontine infarct
- D. A false localising sign of altered ICP
- E. Myasthenic crisis

33. A patient with a large left subdural haematoma has a dilated left pupil and a LEFT hemiparesis. The best explanation is:

- A. Post-ictal Todd paresis
- B. Left PComm artery aneurysm
- C. A right medullary infarct
- D. Kernohan's notch phenomenon
- E. A second, right-sided lesion

34. Which CT sign is the single most useful indicator of impending herniation?

- A. Dilated temporal horn on the side of the mass
- B. Effacement of the basal (perimesencephalic) cisterns
- C. Intraventricular blood
- D. Midline shift of 3 mm at the septum pellucidum
- E. A small contusion in the frontal pole

35. Subfalcine herniation compressing the anterior cerebral artery typically produces:

- A. Bilateral abducens palsies
- B. Ipsilateral oculomotor palsy
- C. Bradycardia and ataxic breathing
- D. Weakness of the contralateral leg
- E. Contralateral homonymous hemianopia

36. A patient with a known mass lesion develops hypertension, bradycardia and irregular breathing. Which response is wrong?

- A. Atropine and an antihypertensive to normalise vitals
- B. Call neurosurgery and arrange CT at the same time
- C. Osmotherapy as a bridge to definitive treatment
- D. Head-up at 30° with the neck kept midline
- E. Avoid hypotension and maintain oxygenation

37. After severe TBI, a patient has episodes of tachycardia, hypertension, sweating, fever and posturing triggered by handling. Pupils and ICP are unchanged. The best treatment approach is:

- A. Urgent osmotherapy for presumed herniation
- B. Repeated changes of broad-spectrum antibiotics
- C. Atropine for each bradycardic episode
- D. Opioids, propranolol, gabapentin or clonidine
- E. Escalation to barbiturate coma

4 RAISED INTRACRANIAL PRESSURE

38. In the compensated phase of an expanding intracranial mass, pressure barely changes mainly because:

- A. CSF production stops almost completely
- B. CSF and venous blood are displaced from the skull
- C. Brain parenchyma compresses by about a fifth
- D. The adult skull sutures allow expansion
- E. Arterial inflow falls in step with the mass

39. A patient has a MAP of 80 mmHg and an ICP of 25 mmHg. The CPP is:

- A. 3.2 mmHg
- B. 45 mmHg
- C. 55 mmHg
- D. 65 mmHg
- E. 105 mmHg

40. A pressure reactivity index (PRx) of +0.4 indicates:

- A. Hyperventilation is safe
- B. Impaired autoregulation
- C. Intact autoregulation
- D. Normal intracranial compliance
- E. CPP at its optimum

41. According to the BTF 4th edition, treatment of raised ICP should start when ICP exceeds:

- A. 15 mmHg
- B. 20 mmHg
- C. 22 mmHg
- D. 25 mmHg
- E. 30 mmHg

42. For a 35-year-old with severe TBI, the BTF systolic blood pressure target is at least:

- A. 90 mmHg
- B. 100 mmHg
- C. 110 mmHg
- D. 120 mmHg
- E. 140 mmHg

43. An external ventricular drain transducer should be zeroed and levelled at the:

- A. Phlebostatic axis (fourth intercostal space)
- B. External auditory meatus (tragus)
- C. Mastoid tip
- D. Sternal angle
- E. Vertex of the skull

44. Which is a limitation of an intraparenchymal ICP transducer compared with an EVD?

- A. It has a higher infection risk
- B. It cannot measure pressure while the patient is supine
- C. It cannot drain CSF or be re-zeroed after insertion
- D. It provides no continuous waveform
- E. It is harder to insert into shifted ventricles

45. The ICP pulse waveform shows P2 higher than P1, with a rounded contour. This suggests:

- A. A blocked or kinked catheter
- B. Over-drainage of CSF from the EVD
- C. Aortic regurgitation artefact
- D. Normal intracranial compliance
- E. Exhausted intracranial compliance

46. Which measure is NOT recommended in the SIBICC algorithm?

- A. Mild hypothermia (35–36 °C) in Tier 3
- B. A MAP challenge to assess autoregulation in Tier 2
- C. A neuromuscular blockade trial in Tier 2
- D. Mannitol by continuous infusion
- E. Mannitol by intermittent bolus in Tier 1

47. A patient with both monitors has an ICP of 15 mmHg and a PbtO₂ of 14 mmHg. The SIBICC approach is to:

- A. Ignore the PbtO₂ because the ICP is normal
- B. Give mannitol
- C. Start barbiturate coma
- D. Hyperventilate to a PaCO₂ of 30 mmHg
- E. Improve oxygen delivery — CPP, FiO₂, haemoglobin

48. A patient with a blown pupil needs urgent osmotherapy but has no central access. A suitable choice is:

- A. 0.45% saline 1 L over one hour
- B. 3% saline 250 mL (or about 5 mL/kg) peripherally
- C. 5% dextrose 500 mL over 20 minutes
- D. 7.5% saline 2 mL/kg via a peripheral cannula
- E. 23.4% saline 30 mL via a peripheral cannula

49. Before a repeat dose of mannitol: measured osmolality 326 mOsm/kg, Na 148, glucose 6 and urea 8 mmol/L. Applying the osmolar-gap rule, the correct decision is:

- A. Withhold — the measured osmolality is above 320
- B. Give double the dose — the gap is low
- C. Withhold — the osmolar gap is 28
- D. Give the dose if indicated — the osmolar gap is 16
- E. Switch to a continuous mannitol infusion

50. Which patient factor favours mannitol over hypertonic saline?

- A. A need for rapid intravascular volume expansion
- B. Acute kidney injury with a rising creatinine
- C. Haemorrhagic shock still being resuscitated
- D. Hypotension with hypovolaemia
- E. Established hypernatraemia of 158 mmol/L

51. What did RESCUEicp show for secondary decompressive craniectomy in refractory ICP above 25 mmHg?

- A. Better function, with no change in mortality
- B. Lower mortality, but more survivors with severe disability
- C. Benefit only if performed within 6 hours of injury, none later
- D. Higher mortality, with no change in disability
- E. No effect on mortality or on functional outcome

52. In the Eurotherm3235 trial, hypothermia to 32–35 °C as a Tier 2 ICP measure:

- A. Was effective only above 35 °C
- B. Reduced mortality but increased disability
- C. Had no effect on ICP
- D. Lowered ICP and improved functional outcome
- E. Lowered ICP but produced worse functional outcome

5 DISEASE-SPECIFIC MANAGEMENT

53. In CRASH-3, tranexamic acid within 3 hours of TBI:

- A. Fewer deaths mainly with bilaterally unreactive pupils
- B. Fewer deaths at all severities, most in severe TBI
- C. Benefit only when given later than 3 hours
- D. More thrombotic events; the trial was stopped early
- E. Fewer head-injury deaths in mild–moderate TBI only

54. A TBI CT shows compressed basal cisterns, a 3 mm midline shift and no lesion over 25 mL. The Marshall category is:

- A. Diffuse injury IV (shift)
- B. Non-evacuated mass lesion (VI)
- C. Diffuse injury III (swelling)
- D. Diffuse injury I
- E. Diffuse injury II

55. A patient with aneurysmal SAH has a GCS of 13 and a hemiparesis. The WFNS grade is:

- A. I
- B. II
- C. III
- D. IV
- E. V

56. Which measure is supported for delayed cerebral ischaemia after aneurysmal SAH?

- A. Statins started on admission, which prevent DCI
- B. Fluid restriction, which lowers the risk of DCI
- C. IV magnesium infusion, which improves functional outcome
- D. Prophylactic triple-H therapy from the day of admission
- E. Induced hypertension for symptomatic DCI, aneurysm secured

57. On day 7 after SAH, the MCA mean velocity is 150 cm/s and the extracranial ICA velocity is 90 cm/s. The best interpretation is:

- A. Hyperaemia, not vasospasm
- B. Cerebral circulatory arrest
- C. Insonation of the wrong vessel
- D. Moderate vasospasm
- E. Severe vasospasm

58. A patient with mild-to-moderate ICH presents with a systolic BP of 190 mmHg. The AHA 2022 target is:

- A. 140 mmHg, kept within 130–150 mmHg
- B. No treatment unless above 220 mmHg
- C. Below 110 mmHg
- D. Below 120 mmHg within the first hour
- E. Below 180 mmHg only

59. A 72-year-old with ICH has GCS 10, a supratentorial haematoma of 40 mL and intraventricular extension. The ICH score is:

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

60. On CT the largest haematoma diameter is 6 cm, the perpendicular is 4 cm, and blood appears on 10 slices of 5 mm. The ABC/2 volume is:

- A. 24 mL
- B. 30 mL
- C. 60 mL
- D. 120 mL
- E. 240 mL

61. A patient on dabigatran has an ICH. The specific reversal agent is:

- A. Fresh frozen plasma 15 mL/kg
- B. Idarucizumab 5 g IV
- C. Protamine 50 mg
- D. Andexanet alfa
- E. Vitamin K 10 mg IV

62. A cerebellar haemorrhage causes falling consciousness and obstructive hydrocephalus. The recommended treatment is:

- A. EVD alone
- B. Conservative care with repeat CT in 24 hours
- C. Surgical evacuation of the haematoma
- D. Lumbar drainage
- E. Osmotherapy alone

63. In patients aged 60 or under with malignant MCA infarction, decompressive hemicraniectomy within 48 hours:

- A. Increases mortality in younger patients
- B. Cuts mortality from about 70% to about 20%
- C. Benefits only patients operated after 96 hours
- D. Is no better than osmotherapy alone
- E. Has no measurable effect on mortality

64. Bacterial meningitis is suspected in a patient with a GCS of 9. What is the correct order?

- A. CT, then LP, then antibiotics
- B. LP, then CT, then antibiotics
- C. Antibiotics, then LP, then dexamethasone 24 hours later
- D. CT, then antibiotics only if CT is normal
- E. Blood cultures, dexamethasone and antibiotics, then CT, then LP

65. A 68-year-old with suspected bacterial meningitis needs empirical therapy. Which agent is added to ceftriaxone specifically because of age?

- A. Fluconazole, for Cryptococcus
- B. Amoxicillin or ampicillin, for Listeria
- C. Metronidazole, for anaerobic cover
- D. Gentamicin, for Pseudomonas cover
- E. Aciclovir, for herpes simplex

66. A patient with suspected HSV encephalitis has a negative CSF PCR taken 24 hours after symptom onset, and suspicion remains high. The correct step is:

- A. Continue aciclovir and repeat the PCR
- B. Stop aciclovir — HSV is excluded
- C. Stop aciclovir and start steroids
- D. Switch to ganciclovir
- E. Continue aciclovir for 48 hours only

67. A young woman has psychiatric symptoms, orofacial dyskinesias, autonomic instability and refractory seizures. Besides immunotherapy, which investigation is essential?

- A. Pelvic imaging for an ovarian teratoma
- B. Testicular ultrasound
- C. Serum copper and caeruloplasmin only
- D. Repeat CT head daily
- E. Muscle biopsy

68. In a patient with Guillain-Barré syndrome, which value is concerning for impending respiratory failure?

- A. Vital capacity of 40 mL/kg
- B. Maximal expiratory pressure of 60 cmH₂O
- C. NIF of -50 cmH₂O
- D. Vital capacity below 20 mL/kg
- E. PaCO₂ of 38 mmHg

69. Which drug is a recognised trigger of myasthenic crisis?

- A. Heparin
- B. Ceftriaxone
- C. Paracetamol
- D. Omeprazole
- E. Gentamicin

70. After two weeks of sepsis and steroids, a patient cannot be weaned. There is limb weakness with reduced reflexes and distal sensory loss; facial and ocular muscles are spared. The most likely diagnosis is:

- A. Botulism
- B. Locked-in syndrome
- C. Guillain-Barré syndrome
- D. Myasthenic crisis
- E. ICU-acquired weakness

71. On day 5 after SAH, sodium falls to 129 mmol/L. Urine output is 4 L/day, the fluid balance is negative and urea is rising. The best management is:

- A. Saline (isotonic or hypertonic) and fludrocortisone
- B. Tolvaptan 15 mg orally, then recheck
- C. Demeclocycline 300 mg twice daily
- D. Fluid restriction to 1 L per day
- E. Furosemide with oral free-water intake

72. A patient with hyponatraemia is having seizures. The initial treatment is:

- A. Fluid restriction to 800 mL/day alone
- B. 3% saline targeting a 20 mmol/L rise in 24 h
- C. 1 L of 0.9% saline over one hour
- D. 150 mL of 3% saline over 20 min, repeated up to twice
- E. Tolvaptan 15 mg orally, then recheck sodium

73. An 80 kg man with central diabetes insipidus has a sodium of 154 mmol/L. His free-water deficit is approximately:

- A. 1.2 L
- B. 2.4 L
- C. 4.8 L
- D. 8.0 L
- E. 10.0 L

6 CONDITIONS THAT HIDE THE EXAMINATION

74. A patient briefly awakens to voice with eye contact lasting less than 10 seconds. The RASS is:

- A. -4
- B. -3
- C. -2
- D. -1
- E. 0

75. CAM-ICU can be assessed only when the RASS is:

- A. +2 or higher
- B. -3 or lighter
- C. 0 exactly
- D. -4 or deeper
- E. Any value, including -5

76. Propofol infusion syndrome is most associated with:

- A. Above ~4 mg/kg/h for more than 48 hours
- B. Co-administration with dexmedetomidine
- C. Any single induction dose of propofol
- D. Use in a patient with egg allergy
- E. Low doses (< 1 mg/kg/h) for 6 hours

77. Which statement about dexmedetomidine in the neuro-ICU is correct?

- A. It is the agent of choice for status epilepticus
- B. It causes marked respiratory depression
- C. It neither lowers ICP nor suppresses seizures
- D. It lowers ICP more than propofol
- E. It accumulates in renal failure more than midazolam

78. A daily sedation hold is contraindicated in which situation?

- A. Renal replacement therapy
- B. A recent tracheostomy
- C. Delirium on CAM-ICU
- D. Mild hypoxaemia on FiO₂ 0.35
- E. Active intracranial hypertension

79. A patient on valproate is encephalopathic with normal liver tests. The most useful next test is:

- A. Creatine kinase
- B. Serum copper
- C. Thyroid function only
- D. Serum ammonia
- E. Serum lithium

80. Which finding best distinguishes serotonin syndrome from neuroleptic malignant syndrome?

- A. Raised creatine kinase
- B. Reduced level of consciousness
- C. Hyperthermia above 39 °C
- D. Clonus and hyperreflexia
- E. Labile blood pressure and heart rate

7 SEIZURES AND STATUS EPILEPTICUS

81. In the landmark series of critically ill patients on continuous EEG, what proportion of the patients who had seizures had purely electrographic seizures?

- A. About 10%
- B. About 25%
- C. About 50%
- D. About 75%
- E. More than 90%

82. A comatose patient's 30-minute routine EEG is normal, but suspicion of NCSE remains. What is the right next step?

- A. Continuous EEG for 48 hours or more
- B. Accept it and look for another cause
- C. Proceed directly to SSEP testing
- D. Repeat a routine EEG in one week
- E. Empirical phenytoin, then no further EEG

83. Under ACNS 2021 terminology, which pattern qualifies as an electrographic seizure?

- A. Periodic discharges at 1 Hz for 10 minutes
- B. Rhythmic delta at 1.5 Hz for 60 s, unchanging
- C. Spike-and-wave at 3 Hz lasting 6 seconds
- D. Spike-and-wave at 2 Hz for 30 s, no evolution
- E. Spike-and-wave at 3 Hz lasting 12 seconds

84. The cEEG shows electrographic seizures totalling 15 minutes in one hour, none lasting longer than 4 minutes. This meets the definition of:

- A. Ictal-interictal continuum
- B. Electroclinical seizure
- C. Isolated electrographic seizures only
- D. Electrographic status epilepticus
- E. Generalised periodic discharges

85. A comatose patient has lateralised periodic discharges at 1.5 Hz. After IV levetiracetam the EEG improves, but the patient's clinical state does not. Under the Salzburg criteria this is:

- A. Certain NCSE
- B. Possible NCSE
- C. Electrographic status epilepticus
- D. Post-anoxic status myoclonus
- E. Excluded NCSE

86. A 70 kg man is in convulsive status epilepticus with IV access. The correct first benzodiazepine dose is:

- A. Lorazepam 4 mg IV
- B. Lorazepam 7 mg IV
- C. Midazolam 2.5 mg IM
- D. Lorazepam 2 mg IV, repeated every 10 minutes
- E. Diazepam 2 mg IV

87. An 80 kg patient needs second-line levetiracetam for status epilepticus. The correct loading dose is:

- A. 1000 mg
- B. 2000 mg
- C. 4500 mg
- D. 4800 mg
- E. 6000 mg

88. In which patient is valproate the least appropriate second-line agent for status epilepticus?

- A. A patient with renal failure
- B. A man with heart block on ECG
- C. A patient with hypotension after phenytoin
- D. An elderly man with a QT interval of 450 ms
- E. A woman with POLG-related mitochondrial disease

89. A patient on valproate for status epilepticus is started on meropenem for sepsis. The expected effect is:

- A. Valproate-induced neutropenia
- B. No interaction
- C. Prolongation of the PR interval
- D. A sharp fall in valproate levels
- E. A sharp rise in valproate levels

8 PROGNOSIS AND COMMUNICATION

90. The ERC/ESICM 2025 neuroprognostication algorithm applies to unconscious patients who, at 72 hours or later, have a GCS motor score of:

- A. 1 only
- B. 3 or less
- C. 4 or less
- D. 5 or less
- E. 6

91. Which of the following is an ERC/ESICM 2025 indicator of good outcome after cardiac arrest?

- A. NSE of 17 µg/L or less within 72 hours
- B. Burst-suppression at 36 hours
- C. Bilaterally present N20 SSEP responses
- D. NSE above 60 µg/L at 48 hours
- E. Status myoclonus at 24 hours

92. Which finding is NOT one of the ERC/ESICM 2025 predictors of poor outcome?

- A. Absent pupillary and corneal reflexes at ≥ 72 hours
- B. Bilaterally absent N20 SSEP at ≥ 24 hours
- C. Absent motor response to pain at 72 hours
- D. Status myoclonus within 72 hours
- E. Suppressed or burst-suppression EEG at > 24 hours

93. At 72 hours after cardiac arrest, NSE is 74 µg/L in a haemolysed sample. Pupillary and corneal reflexes are intact and the EEG is continuous. The outcome is:

- A. Indeterminate — repeat NSE, continue full care
- B. Good — a continuous EEG overrides NSE
- C. Poor — one predictor suffices after 72 h
- D. Indeterminate — withdraw if NSE rises
- E. Poor — NSE above 60 µg/L is diagnostic

94. What is the main defence against the self-fulfilling prophecy in neuroprognostication?

- A. Rely on the single most specific predictor available
- B. Apply one prognostic score to every condition
- C. Wait, clear confounders, and require concordant modalities
- D. Decide within 24 hours, before the family is attached
- E. Withdraw care when any single predictor is abnormal

95. In a family meeting about an uncertain prognosis, which question best reflects good practice?

- A. "What would he say about living with this level of disability?"
- B. "His GCS is 5 — do you understand what that means?"
- C. "There is nothing more we can do — do you agree?"
- D. "Shall we stop all of his treatment now, then?"
- E. "Do you want us to do everything possible for him?"

9 DEATH BY NEUROLOGICAL CRITERIA

96. Which is a prerequisite for adult determination of death by neurological criteria under AAN 2023?

- A. Core temperature of at least 36 °C
- B. A normal serum sodium of 135–145 mmol/L exactly
- C. Core temperature of at least 34 °C
- D. No vasopressor support
- E. At least 72 hours after cardiac arrest in all cases

97. During an apnoea test, baseline PaCO₂ is 40 mmHg. Which result is consistent with death by neurological criteria?

- A. SpO₂ falls to 80% and the test is stopped at 4 minutes
- B. PaCO₂ 58 mmHg with no respiratory effort
- C. PaCO₂ 62 mmHg with no respiratory effort
- D. PaCO₂ 55 mmHg with no respiratory effort
- E. PaCO₂ 70 mmHg with one shallow breath

98. Under AAN 2023, which ancillary test is accepted for adult determination of death by neurological criteria?

- A. CT angiography
- B. Bispectral index monitoring
- C. Somatosensory evoked potentials
- D. EEG
- E. Radionuclide perfusion scintigraphy

99. During assessment for brain death, the patient develops triple flexion of the legs to nail-bed pressure. This:

- A. Proves the patient is in a minimally conscious state
- B. Means the apnoea test must be skipped
- C. Excludes brain death
- D. Is a spinal reflex and does not exclude the diagnosis
- E. Indicates residual midbrain function

100. A haemodialysis patient on baclofen is comatose with absent brainstem reflexes and a normal CT. What is the correct conclusion?

- A. Declare death after one examination
- B. Not met — manage as baclofen toxicity
- C. Proceed to radionuclide scintigraphy
- D. Proceed to the apnoea test as planned
- E. Confirm death with a single EEG

ANSWERS AND EXPLANATIONS

1 A	2 C	3 D	4 A	5 A	6 E	7 B	8 C	9 E	10 B
11 C	12 E	13 E	14 B	15 D	16 E	17 E	18 D	19 A	20 D
21 A	22 D	23 C	24 B	25 B	26 A	27 B	28 D	29 A	30 B
31 B	32 D	33 D	34 B	35 D	36 A	37 D	38 B	39 C	40 B
41 C	42 C	43 B	44 C	45 E	46 D	47 E	48 B	49 D	50 E
51 B	52 E	53 E	54 C	55 C	56 E	57 A	58 A	59 C	60 C
61 B	62 C	63 B	64 E	65 B	66 A	67 A	68 D	69 E	70 E
71 A	72 D	73 C	74 C	75 B	76 A	77 C	78 E	79 D	80 D
81 E	82 A	83 E	84 D	85 B	86 A	87 C	88 E	89 D	90 D
91 A	92 C	93 A	94 C	95 A	96 A	97 C	98 E	99 D	100 B

1 — A. Upper brainstem tegmentum or both thalami. The arousal generator sits above the mid-pons, and its relay is the diencephalon. Lesions below the mid-pons spare consciousness (think locked-in syndrome), and a unilateral hemispheric lesion almost never causes coma on its own. (p. 9)

2 — C. Minimally conscious state minus (MCS-). Visual pursuit is a non-linguistic sign of awareness, so the patient is in MCS-. MCS+ needs language-related behaviour such as command following or intelligible words. (p. 8)

3 — D. Functional use of two different objects. Emergence needs functional communication or functional use of two objects. Command following and intelligible words mark MCS+, and pursuit and localisation mark MCS-. (p. 8)

4 — A. The highest item reached on each subscale. The CRS-R is hierarchical. The diagnosis follows the highest item achieved on each of the six subscales, not the total out of 23. (p. 13)

5 — A. About one in four. About a quarter had cognitive motor dissociation. It was more common in younger patients and after traumatic injury, which is why behavioural unresponsiveness does not prove absent awareness. (p. 13)

6 — E. 100–200 mg twice daily, weeks 4–16 after injury. The AAN 2018 recommendation rests on a randomised trial of amantadine 100–200 mg twice daily given 4–16 weeks after traumatic injury. (p. 13)

7 — B. Locus coeruleus (noradrenaline, α_2 receptors). Dexmedetomidine is an α_2 agonist acting on the pontine locus coeruleus. Histamine and orexin systems explain antihistamine sedation and narcolepsy. (p. 10)

8 — C. Artery of Percheron infarction (both thalami). A few millilitres of infarct at the thalamic relay can cause coma. Symmetry and a normal early CT are not reassuring when the eyes point to the diencephalon; MRI with DWI is the test. (p. 9)

9 — E. Cefepime toxicity plus morphine metabolite build-up. Both are reversible causes in renal failure, and they often coexist. The EEG typically shows generalised periodic discharges with triphasic morphology, which resolve when cefepime is switched. (p. 12)

10 — B. E2 VT M3. Report the components and mark the verbal score as not testable. A summed score containing an artificial V1 is misleading. (p. 16)

11 — C. 5. GCS-P = GCS – Pupil Reactivity Score, where the PRS is the number of unreactive pupils (0–2). So $6 - 1 = 5$. (p. 16)

12 — E. Motor response. E1V1M5 and E3V2M2 both total 7, but the first localises and the second extends. The motor score drives the prognostic models. (p. 16)

13 — E. A fall of 1 point in the motor score. A 1-point motor fall, or a fall of 2 or more in the total, is deterioration: examine the pupils, call a senior and repeat imaging. (p. 16)

14 — B. R1. R1 means breathing above the ventilator rate. Breathing at the set rate, or apnoea, scores R0, which does not establish apnoea — that needs a formal test. (p. 17)

15 — D. B3. B4 = pupil and corneal reflexes present; B3 = one pupil wide and fixed; B2 = pupil or corneal reflexes absent; B1 = both absent; B0 = pupil, corneal and cough absent. (p. 17)

16 — E. A prompt to consider brain death testing only. FOUR 0 is the only score that prompts consideration of DNC testing. Determination needs the prerequisites, the full examination and an apnoea test. (p. 17)

17 — E. Left optic nerve. Paradoxical dilation when the light reaches one eye means reduced afferent input from that eye. The test needs only one working iris. (p. 18)

18 — D. High-dose barbiturates. The light reflex is one of the last functions lost to metabolic suppression. The exceptions are hypothermia, anticholinergic toxicity, high-dose barbiturates and deep anaesthesia. (p. 15)

19 — A. Abnormal — interocular difference ≥ 0.7 . By convention NPi ≥ 3 is normal and < 3 abnormal. A difference of ≥ 0.7 between eyes is also abnormal, and a falling trend is an early warning. (p. 19)

20 — D. Pharmacological blockade of the iris. A compressed third nerve still constricts to pilocarpine because the sphincter receptors are intact; a pharmacologically blocked iris does not. The scan correctly came first. (p. 19)

21 — A. Above the midbrain (hemispheres or diencephalon). Abnormal (decorticate) flexion implies dysfunction above the midbrain. Extension generally implies a lower or more severe dysfunction — midbrain–upper pons, or severe metabolic coma. (p. 20)

22 — D. Supraorbital or trapezius pressure. A peripheral stimulus can provoke only a spinal withdrawal. Localisation needs a central stimulus — trapezius pinch or supraorbital pressure; sternal rub is poorly standardised and bruises. (p. 14)

23 — C. Mid–lower pons. Cheyne–Stokes: hemispheric or diencephalic; central neurogenic hyperventilation: midbrain–upper pons; apneustic: mid–lower pons; cluster: lower pons–upper medulla; ataxic: medulla. (p. 21)

24 — B. V₁ afferent → VII efferent, pons. The corneal reflex runs from the ophthalmic division of the trigeminal nerve to the facial nerve through the pons. Use a cotton wisp or saline on the cornea, not the sclera. (p. 22)

25 — B. Cough to deep tracheal suction. The gag is often weak in normal elderly people and hard to judge with some tubes. Cough to suction at the carina is the better medullary test. (p. 22)

26 — A. Intact brainstem gaze pathways, no cortical correction. In coma with an intact brainstem the eyes drift tonically toward the cold ear. Nystagmus with a fast phase away from the cold ear means the cortex is working. (p. 24)

27 — B. Working cortex — consider psychogenic coma. The corrective fast phase is generated by the cortex. Its presence is incompatible with true coma. (p. 24)

28 — D. A pontine lesion on the side opposite the hemiparesis. A destructive frontal lesion drives the eyes toward the lesion, away from the hemiparesis. A pontine lesion, a seizure focus or a thalamic haemorrhage ("wrong-way eyes") can drive them toward the weak side. (p. 24)

29 — A. Extensive pontine lesions. This is ocular bobbing. Roving eye movements suggest an intact brainstem, and ping-pong gaze suggests bilateral hemispheric dysfunction. (p. 24)

30 — B. Contralateral hemiparesis. The pyramids are medial, so lateral medullary infarction causes no hemiparesis — the crossing is sensory. Hemiparesis with an ipsilateral XII palsy is the medial medullary syndrome. (p. 25)

31 — B. Left hypoglossal nerve or nucleus (lower motor neuron). With a lower motor neuron XII lesion the tongue points toward the lesion. With an upper motor neuron lesion it points away from the lesion. (p. 25)

32 — D. A false localising sign of altered ICP. The abducens nerve has a long intracranial course and is stretched over the petrous apex when ICP rises or falls, including after LP or CSF over-drainage. (p. 26)

33 — D. Kernohan's notch phenomenon. Midline shift pushes the opposite peduncle against the tentorial edge, giving hemiparesis on the side of the mass. The pupil is the more reliable sign of the side of the lesion. (p. 26)

34 — B. Effacement of the basal (perimesencephalic) cisterns. Effaced basal cisterns are the most useful single sign. A midline shift of more than 5 mm is significant in TBI guidelines. (p. 27)

35 — D. Weakness of the contralateral leg. The cingulate gyrus slides under the falx; it is often silent but can occlude the ACA. PCA compression in uncus herniation causes occipital infarction. (p. 27)

36 — A. Atropine and an antihypertensive to normalise vitals. The Cushing response is a late, pre-terminal brainstem reflex defending perfusion. Treat the pressure, not the blood pressure or heart rate in isolation. (p. 28)

37 — D. Opioids, propranolol, gabapentin or clonidine. This is paroxysmal sympathetic hyperactivity. Unlike Cushing's response, heart rate rises. Exclude seizures, sepsis, pain and withdrawal first. (p. 28)

38 — B. CSF and venous blood are displaced from the skull. Monro-Kellie: brain about 80%, blood 10%, CSF 10%. Once the CSF and venous buffers are spent, the pressure-volume curve becomes exponential. (p. 29)

39 — C. 55 mmHg. CPP = MAP – ICP. A CPP of 55 is below the BTF target of 60–70 mmHg. (p. 29)

40 — B. Impaired autoregulation. PR_x is negative or near zero when vessels react. Values above about +0.2 to +0.3 are regarded as impaired. CPP_{opt} is the minimum of the PR_x–CPP curve. (p. 30)

41 — C. 22 mmHg. BTF 4th edition (level IIB) uses > 22 mmHg. Act on sustained rises, not brief spikes from coughing. (p. 33)

42 — C. 110 mmHg. SBP ≥ 110 mmHg for ages 15–49 or over 70; ≥ 100 mmHg for ages 50–69. A single episode of SBP < 90 mmHg is associated with substantially worse outcome. (p. 33)

43 — B. External auditory meatus (tragus). The tragus is the surrogate for the foramen of Monro. Re-level after every change of position. (p. 31)

44 — C. It cannot drain CSF or be re-zeroed after insertion. Intraparenchymal devices are easy to insert with low infection and haemorrhage risk. But they drift, measure local pressure, and cannot drain. (p. 31)

45 — E. Exhausted intracranial compliance. Normally P₁ > P₂ > P₃. P₂ reflects brain compliance, and its rise above P₁ can precede a rise in mean ICP. (p. 32)

46 — D. Mannitol by continuous infusion. SIBICC also advises against scheduled hypertonic infusions to raise sodium, lumbar CSF drainage, routine PaCO₂ < 30 mmHg, CPP > 90 mmHg and routine steroids. (p. 34)

47 — E. Improve oxygen delivery — CPP, FiO₂, haemoglobin. PbtO₂ < 20 mmHg is the treatment threshold. Low PbtO₂ with normal ICP calls for measures that raise oxygen delivery, not ICP-lowering therapy. (p. 34)

48 — B. 3% saline 250 mL (or about 5 mL/kg) peripherally. 23.4% saline needs a central line. Mannitol 20% at 1 g/kg is an alternative if the patient is not hypovolaemic. Hypotonic and glucose-containing fluids are avoided. (p. 35)

49 — D. Give the dose if indicated — the osmolar gap is 16. Calculated osmolality = 2 × 148 + 6 + 8 = 310; gap = 326 – 310 = 16. A gap above 20 means mannitol is accumulating. The 320 ceiling is the weaker guide. (p. 36)

50 — E. Established hypernatraemia of 158 mmol/L. Hypertonic saline expands volume and suits hypotension and renal impairment. Mannitol suits volume overload or established hypernatraemia above 155–160. (p. 36)

51 — B. Lower mortality, but more survivors with severe disability. RESCUEicp: secondary craniectomy for refractory ICP > 25 mmHg cut 6-month mortality (about 27% vs 49%) but left more survivors vegetative or severely disabled. DECRA (early bifrontal craniectomy for moderate ICP elevation) worsened functional outcome. Lowering ICP and improving outcome are different things. (p. 37)

52 — E. Lowered ICP but produced worse functional outcome. As a result, SIBICC places only mild hypothermia (35–36 °C) in Tier 3. Fever prevention is the routine target. (p. 37)

53 — E. Fewer head-injury deaths in mild-moderate TBI only. TXA 1 g over 10 minutes then 1 g over 8 hours; earlier treatment was more effective. No benefit was seen with bilaterally unreactive pupils. (p. 38)

54 — C. Diffuse injury III (swelling). Compressed or absent cisterns with a shift of 0–5 mm is III. A shift above 5 mm is IV. (p. 38)

55 — C. III. WFNS: I = GCS 15; II = 13–14 without deficit; III = 13–14 with deficit; IV = 7–12; V = 3–6. (p. 39)

56 — E. Induced hypertension for symptomatic DCI, aneurysm secured. For symptomatic DCI with a secured aneurysm, induced hypertension is reasonable (AHA 2023, weak recommendation). Maintain euvolaemia; prophylactic triple-H, magnesium and statins are not recommended. (p. 40)

57 — A. Hyperaemia, not vasospasm. The Lindegaard ratio is 150/90 ≈ 1.7. A ratio above 3 suggests vasospasm and above 6 severe spasm; a high MCA velocity with a low ratio reflects increased flow. (p. 40)

58 — A. 140 mmHg, kept within 130–150 mmHg. Lowering systolic below 130 mmHg in this group is potentially harmful. Use smooth infusions, not repeated boluses. (p. 41)

59 — C. 3. GCS 5–12 = 1; volume ≥ 30 mL = 1; IVH = 1; infratentorial = 0; age < 80 = 0. Score 3 had 72% 30-day mortality in the derivation cohort — but it should not be used alone to limit care. (p. 41)

60 — C. 60 mL. A = 6, B = 4, C = 10 × 0.5 = 5 cm. Volume ≈ 6 × 4 × 5 ÷ 2 = 60 mL. (p. 41)

61 — B. Idarucizumab 5 g IV. Andexanet (or 4-factor PCC) is used for apixaban and rivaroxaban. Warfarin needs 4-factor PCC plus vitamin K. (p. 41)

62 — C. Surgical evacuation of the haematoma. Evacuate rather than drain alone. An EVD alone in a posterior fossa mass risks upward herniation. (p. 41)

63 — B. Cuts mortality from about 70% to about 20%. Pooled DECIMAL, DESTIAL and HAMLET: absolute mortality reduction ≈ 50% (NNT ≈ 2), with more survivors at moderate disability. Over 60, surgery still improves survival but most survivors are dependent — discuss values before, not after. (p. 42)

64 — E. Blood cultures, dexamethasone and antibiotics, then CT, then LP. GCS < 10 is an indication for CT before LP. But if CT comes first, treatment comes first too. Dexamethasone goes with or just before the first antibiotic dose. (p. 43)

65 — B. Amoxicillin or ampicillin, for Listeria. Listeria risk factors are age over 50, immunocompromise, pregnancy and alcohol dependence. Vancomycin is added where pneumococcal cephalosporin resistance is a concern. (p. 43)

66 — A. Continue aciclovir and repeat the PCR. An early negative PCR (within 72 hours) can be falsely negative. Aciclovir is 10 mg/kg every 8 hours, adjusted for renal function; confirmed HSV is treated for 14–21 days. (p. 43)

67 — A. Pelvic imaging for an ovarian teratoma. This is anti-NMDA receptor encephalitis. Start first-line immunotherapy once infection is reasonably excluded; do not wait for antibody results. (p. 43)

68 — D. Vital capacity below 20 mL/kg. The 20/30/40 rule: VC < 20 mL/kg (or a fall above 30%), NIF weaker than –30 cmH₂O, MEP < 40 cmH₂O. Gas exchange stays normal until late. (p. 44)

69 — E. Gentamicin. Aminoglycosides, fluoroquinolones, macrolides, magnesium, β-blockers and steroid initiation can all precipitate crisis. (p. 44)

70 — E. ICU-acquired weakness. Myasthenia spares reflexes and sensation, with prominent ocular and bulbar signs. GBS develops over days to four weeks, often with facial involvement and raised CSF protein. (p. 44)

71 — A. Saline (isotonic or hypertonic) and fludrocortisone.

This is cerebral salt wasting: volume depletion is the defining feature. Fluid restriction in the DCI window increases ischaemic risk. (p. 45)

72 — D. 150 mL of 3% saline over 20 min, repeated up to twice.

Then limit the rise to 10 mmol/L in the first 24 hours and 8 mmol/L in each following 24 hours. Aim lower when osmotic demyelination risk is high. (p. 45)

73 — C. 4.8 L. Total body water ≈ 0.6 × 80 = 48 L. Deficit = 48 × (154 ÷ 140 – 1) = 4.8 L, replaced over 24–48 hours plus ongoing losses, with desmopressin. (p. 45)

74 — C. –2. –1 is sustained awakening with eye contact ≥ 10 s. –3 is movement or eye opening to voice without eye contact. (p. 46)

75 — B. –3 or lighter. At RASS –4 or –5 the patient cannot engage, so CAM-ICU needs RASS –3 or lighter. Delirium = feature 1 (acute change or fluctuation) + feature 2 (inattention) + either 3 (altered level of consciousness) or 4 (disorganised thinking). (p. 46)

76 — A. Above ~4 mg/kg/h for more than 48 hours. Watch lactate, CK, triglycerides, the ECG and rising vasopressor requirements. (p. 47)

77 — C. It neither lowers ICP nor suppresses seizures. Its advantages are rousable sedation, less delirium and no respiratory depression. Its catches are bradycardia and hypotension. (p. 47)

78 — E. Active intracranial hypertension. Do not hold during active raised ICP, status epilepticus, neuromuscular blockade or severe refractory hypoxaemia. With an ICP monitor, a sustained rise above threshold ends the hold. (p. 47)

79 — D. Serum ammonia. Valproate hyperammonaemia occurs with normal liver tests. Treat with carnitine and stop valproate. (p. 48)

80 — D. Clonus and hyperreflexia. NMS causes lead-pipe rigidity with slow onset after an antipsychotic. Serotonin syndrome causes clonus, hyperreflexia and mydriasis; treat with cyproheptadine. (p. 48)

81 — E. More than 90%. About one in five monitored patients had seizures, and over 90% of those had no clinical signs. (p. 49)

82 — A. Continuous EEG for 48 hours or more. About one in five monitored patients had seizures, over 90% non-convulsive. Roughly a fifth of comatose patients had their first seizure detected only after 24 hours, so at least 48 hours of cEEG is advised in coma. (p. 49)

83 — E. Spike-and-wave at 3 Hz lasting 12 seconds. An electrographic seizure is epileptiform discharges averaging > 2.5 Hz for ≥ 10 s, or any pattern with definite evolution for ≥ 10 s. Slower or shorter patterns may sit on the ictal-interictal continuum. (p. 50)

84 — D. Electrographic status epilepticus. 15 minutes is 25% of the hour, above the 20% threshold. Status is ≥ 10 continuous minutes or ≥ 20% of any 60-minute period. (p. 50)

85 — B. Possible NCSE. Discharges ≤ 2.5 Hz need EEG and clinical improvement together, subtle ictal phenomena, or typical evolution to confirm NCSE. EEG improvement alone makes NCSE possible. (p. 50)

86 — A. Lorazepam 4 mg IV. Lorazepam 0.1 mg/kg, maximum 4 mg per dose, may be repeated once. Small repeated doses are the commonest error; draw up the second-line drug at the same time. (p. 51)

87 — C. 4500 mg. 60 mg/kg would be 4800 mg, but the maximum is 4500 mg. In ESETT, levetiracetam, fosphenytoin and valproate were similarly effective — about half of patients stopped seizing. (p. 51)

88 — E. A woman with POLG-related mitochondrial disease. Avoid valproate in liver disease, pregnancy and mitochondrial disease. Fosphenytoin causes hypotension and arrhythmia. (p. 51)

89 — D. A sharp fall in valproate levels. Carbapenems lower valproate levels sharply, and seizure recurrence follows. Choose a different antibiotic or antiseizure drug. (p. 52)

90 — D. 5 or less. The 2021 entry criterion was motor ≤ 3 . In 2025 it widened to ≤ 5 , and indicators of good outcome were added. (p. 54)

91 — A. NSE of 17 $\mu\text{g/L}$ or less within 72 hours. Good-outcome indicators: GCS motor 4 or 5, a continuous normal-voltage EEG within 72 hours, NSE $\leq 17 \mu\text{g/L}$ within 72 hours, and no diffusion restriction on MRI at 2–7 days. A present N20 does not predict good outcome. (p. 54)

92 — C. Absent motor response to pain at 72 hours. The motor score is the entry criterion, not a poor-outcome predictor. The others, with NSE $> 60 \mu\text{g/L}$ and diffuse anoxic injury on imaging, are the six predictors; two or more are needed. (p. 55)

93 — A. Indeterminate — repeat NSE, continue full care. Haemolysis falsely raises NSE. One doubtful predictor with none concordant is indeterminate, and indeterminate means continue supportive care and reassess. (p. 55)

94 — C. Wait, clear confounders, and require concordant modalities. Withdrawal based on a predictor makes that predictor look perfect. The defence is procedural: wait, clear confounders, use concordant modalities, document the reasoning. (p. 53)

95 — A. "What would he say about living with this level of disability?". Shift the burden from what the family wants to what the patient would want. Describe function, not scores, and name the date of the next reassessment. (p. 57)

96 — A. Core temperature of at least 36 °C. Temperature ≥ 36 °C; SBP ≥ 100 or MAP ≥ 75 mmHg (vasopressors permitted); at least 24 hours after hypoxic–ischaemic injury; no CNS depressant or neuromuscular blocking effect; no confounding metabolic derangement. (p. 58)

97 — C. PaCO₂ 62 mmHg with no respiratory effort. The target is PaCO₂ ≥ 60 mmHg and ≥ 20 mmHg above baseline, with no effort. Any breath excludes DNC; an aborted test needs an ancillary study. (p. 60)

98 — E. Radionuclide perfusion scintigraphy. Accepted: four-vessel catheter angiography, radionuclide perfusion ("hollow skull") and, with expertise, transcranial Doppler. EEG and SSEP test the cortex or pathways rather than whole-brain flow; CT/MR angiography are not recommended in AAN 2023 but appear in some national protocols. (p. 61)

99 — D. Is a spinal reflex and does not exclude the diagnosis. Triple flexion, plantar responses, finger jerks, the Lazarus sign, sweating and tachycardia can occur after brain death. They need judgement by an experienced examiner. (p. 59)

100 — B. Not met — manage as baclofen toxicity. Baclofen accumulates in renal failure and can abolish all brainstem reflexes. With no catastrophic structural cause, determination cannot begin; this patient woke after dialysis. (p. 59)

When a patient in intensive care will not wake up — what is broken, where is it, and what must be done in the next five minutes?

The *Neurocritical Guide* is a bedside reference for physicians and nurses caring for the unresponsive patient. It moves from the physiology of consciousness to the structured examination, brainstem localisation, raised intracranial pressure, disease-specific management, the conditions that hide the examination, seizures, prognosis and the determination of death by neurological criteria.

Every threshold and dose is tied to a numbered reference. Where guidelines disagree, the disagreement is shown. Red boxes mark what must be done now; star boxes mark what to carry to the next patient.

9

CHAPTERS ·
CONSCIOUSNESS TO
DEATH BY NEUROLOGICAL
CRITERIA

4

APPENDICES ·
DOCUMENTATION, DRUGS,
BEDSIDE CARDS, SELF-
ASSESSMENT

1

REFERENCE LIST · IN
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