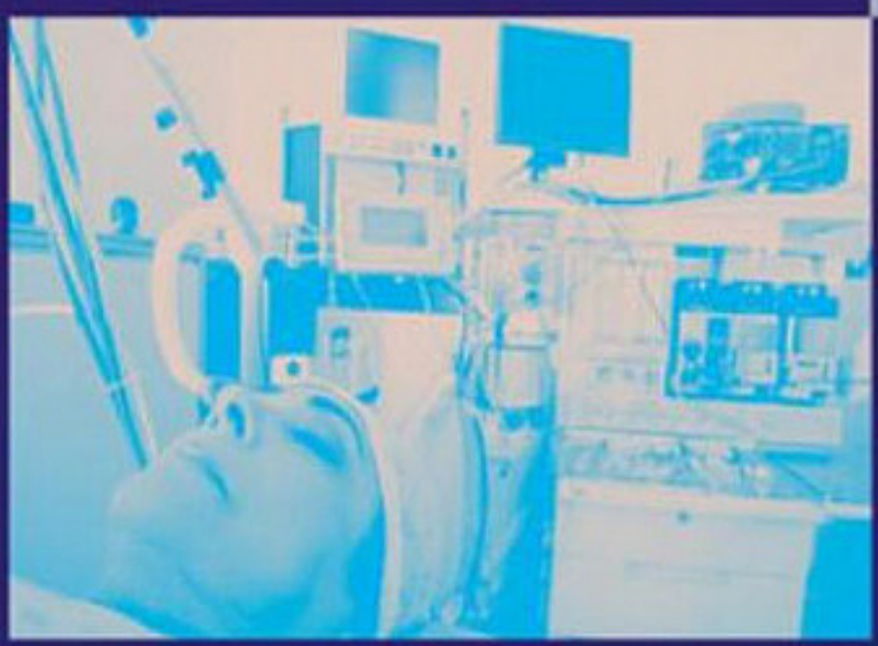
Edited by MICHEL T. TORBEY

Neurocritical Care

SECOND EDITION



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Neurocritical Care

Second Edition

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Edited by
Michel T. Torbey
Department of Neurology, University of New Mexico

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Contributors

Sarah M. Adriance, PharmD, BCPS
Specialty Practice Pharmacist, Neurocritical Care, Department of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, OH, USA

Naeem A. Ali, MD
The Ohio State University Wexner Medical Center, Columbus, OH, USA

Fawaz Al-Mufti, MD
Department of Neurology, Robert Wood Johnson University Hospital, New Brunswick, NJ, USA

Abdo Barakat, MD
University of Minnesota, Anesthesiology Department, MN, USA

Julian Bösel, MD
Department of Neurology, Klinikum Kassel, Kassel, Germany

Xuemei Cai, MD
Massachusetts General Hospital, Boston, MA, USA

Rafael A. Calderón Candelario, MD, MSc
University of Miami, Miller School of Medicine, Miami, FL, USA

Farrukh S. Chaudhry, MD
Department of Neurology and Rehabilitation, The University of Illinois College of Medicine, Chicago, IL, USA

Veronica L. Chiang, MD
Yale-New Haven Hospital, Yale University, New Haven, CT, USA

Jan Claassen, MD, PhD, FNCS
Neurological Intensive Care Unit, Columbia University College of Physicians and Surgeons, New York, NY, USA

Mohit Datta, MD
Palmetto Health USC, Columbia, SC, USA

Indira De Jesus, MD
Neurology, Christiana Care Health System, De, USA

Andrew Demchuk, MD, FRCPC
Department of Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada

Rajat Dhar, MD
Department of Neurology (Division of Neurocritical Care), Washington University in St. Louis, Saint Louis, MO, USA

Michael Diringer, MD
Department of Neurology (Division of Neurocritical Care), Washington University in St. Louis, Saint Louis, MO, USA

Matthew C. Exline, MD
The Ohio State University Wexner Medical Center, Columbus, OH, USA

Michael Frank, MD
Medical College of Wisconsin, Milwaukee, WI, USA

Romergryko G. Geocadin, MD
Johns Hopkins Medical Institutions, Baltimore, MD, USA

Shivani Ghosal, MD
New York-Presbyterian Hospital, New York, NY, USA

Joao A. Gomes, MD
Lerner College of Medicine, Cerebrovascular Center, Cleveland Clinic, Cleveland, OH, USA

Mary Beth Graham, MD
Medical College of Wisconsin, Milwaukee, WI, USA

Ryan A. Grant, MD, MS
Yale-New Haven Hospital, Yale University, New Haven, CT, USA

Diana Greene-Chandos, MD
Department of Neurology and Neurosurgery, Cerebrovascular and Neurocritical Care Division, The Ohio State University, College of Medicine, Columbus, OH, USA

David M. Greer, MD, MA, FCCM, FAHA, FNCS
Boston University, Boston, MA, USA

Noah Grose, RN, BSN, MSN, ACNP-BC
The Ohio State University Wexner Medical Center, Columbus, OH, USA

Nabil Haddad, MD
The Ohio State University Wexner Medical Center, Columbus, OH, USA

Yousef Hannawi, MD
Division of Cerebrovascular Diseases and Neurocritical Care, Department of Neurology, The Ohio State University, Columbus, OH, USA

Archana Hinduja, MD
Department of Neurology, Cerebrovascular and Neurocritical Care Division, The Ohio State University, College of Medicine, Columbus, OH, USA

Mahmoud Houmsse, MD, FACP, FACC
The Ohio State University Wexner Medical Center, Columbus, OH, USA

Lauren Koffman, DO
Department of Neurology, Rush University Medical Center, Chicago, IL, USA

Christopher L. Kramer, MD
Department of Neurology and Surgery (Neurosurgery), University of Chicago Medical Center, Chicago, IL, USA

Mark M. Landreneau, MD
Yale University School of Medicine, New Haven, CT, USA

Peter Le Roux, MD, FACS
Brain and Spine Center, Lankenau Medical Center, Wynnewood, PA, USA

John J. Lewin III, PharmD, MBA, FASHP, FCCM
Departments of Pharmacy, Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD, USA

Geoffrey S. F. Ling, MD, PhD, FAAN, FANA
Departments of Anesthesiology and Critical Care Medicine and Neurology, Johns Hopkins Medical Institutions, Baltimore, Department of Neurology, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Edward M. Manno, MD
Department of Neurology, Feinberg School of Medicine, Northwestern University, IL, USA

Stephan A. Mayer, MD, FCCM
Department of Neurology, Henry Ford Health System, Detroit, MI, USA

Chad M. Miller, MD
Neurocritical Care, Riverside Methodist Hospital, Columbus, OH, USA

Martin M. Monti, PhD
Department of Psychology, University of California Los Angeles, Department of Neurosurgery, David Geffen School of Medicine at University of California Los Angeles, CA, USA

Maximilian Mulder, MD
Abbott Northwestern Hospital, Minneapolis, MN, USA

Barnett R. Nathan, MD
Departments of Neurology and Internal Medicine, University of Virginia, Charlottesville, VA, USA

Anh T. Nguyen, MD
Neurologic Institute, Houston Methodist Hospital, Houston, TX, USA

Kristine O'Phelan, MD
University of Miami Hospital, Miami, FL, USA

Efstathios Papavassiliou, MD
Department of Neurosurgery, Beth Israel Deaconess Hospital, Boston, MA, USA

Dilesh Patel, MD
Ohio State University Wexner Medical Center, Columbus, OH, USA

Jason Prosek, MD
Ohio State University Wexner Medical Center, Columbus, OH, USA

Alejandro A. Rabinstein, MD
Mayo Clinic, Rochester, MN, USA

Andy J. Redmond, MD
Christus Mother Frances Hospital-Tyler, Tyler, TX, USA

Fred Rincon, MD, MSc, MBEthics, FACP, FCCP, FCCM, FNCS
Thomas Jefferson University, Philadelphia, PA, USA

Stephen M. Riordan, MBBS (Hons), MD, FRACP, FRCP
Gastrointestinal and Liver Unit, Prince of Wales Hospital and Prince of Wales Clinical School, University of New South Wales, Sydney, Australia

Jonathan Rosand, MD, MSc
Neuroscience and Intensive Care Unit, Massachusetts General Hospital, Boston, MA, USA

Maher Saqqur, MD, MPH, FRCPC
Department of Medicine, Division of Neurology, University of Alberta, Edmonton, Alberta, Canada

Murat Sari, MD
Department of Neurology, Cerebrovascular and Neurocritical Care Division, The Ohio State University, College of Medicine, Colombus, OH, USA

Caroline Schnakers, PhD
Department of Psychology, University of California Los Angeles, Department of Neurosurgery, David Geffen School of Medicine at University of California, Los Angeles, CA, USA

David B. Seder, MD, FCCP, FCCM
Department of Critical Care Services, Maine Medical Center, Portland, ME, USA

Magdy Selim, MD, PhD
Beth Israel Deaconess Medical Center / Harvard Medical School, Boston, MA, USA

Mohamed Sharaby, MD
Neurocritical Care, University of Virginia Health System, Charlottesville, VA, USA

Kevin N. Sheth, MD, FAHA, FCCM, FNCS, FAAN, FANA
Department of Neurology, Yale New Haven Hospital, New Haven, CT, USA

Michel T. Torbey, MD, MPH, FCCM, FAHA
Department of Neurology, The University of New Mexico, Albuquerque, NM, USA

Panayiotis N. Varelas, MD, PhD
Departments of Neurology and Neurosurgery, Henry Ford Hospital, Detroit, MI, USA

Katja E. Wartenberg, MD, PhD
University of Leipzig, Leipzig, Germany

Sara T. R. Widing, MHA
Joe DiMaggio Children's Hospital, Orlando, FL, USA

Roger Williams CBE, MD, FRCP, FRCS, FRCPE, FRACP, F Med Sci, FRCPI (Hon), FACP (Hon)
Institute of Hepatology, Foundation for Liver Research, London, and Faculty of Life Sciences and Medicine, King's College, London, UK

Karina Woodling, MD
Department of Neurology, Cerebrovascular and Neurocritical Care Division, Ohio State University, College of Medicine, Columbus, OH, USA

Wendy Wright, MD, FCCM, FNCS
Emory University School of Medicine, Atlanta, GA, USA

Xiaomeng Xu, PhD
Beth Israel Deaconess Medical Center, Boston, MA, USA

Xiaoying Yao, MD
El Camino Hospital, Mountain View, CA, USA

Asma Zakaria, MD
Division of Medical Critical Care Services,
Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA

Wendy C. Ziai, MD, MPH
Division of Neurosciences Intensive Care, Department of Anesthesiology and Critical Care Medicine and
Department of Neurology, Johns Hopkins University, Baltimore, MD, USA

David Zygun, MD, MSc, FRCPC
Departments of Critical Care Medicine, Clinical Neurosciences and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada

Preface

Management of critically ill neurologic and neurosurgical patients can be challenging. The complexity of the brain and how it reacts to different physiological stressors continues to present itself as a black box, even to the seasoned intensivist. The "Neurocritical Care" book has been produced to provide all healthcare professionals caring for critically ill neurologic and neurosurgical patients with a straightforward, concise, and practical reference to assist them with management decisions.

A lot of changes in the field of neurocritical care have happened since the first edition of the book. Neurocritical care units exist now in most academic centers. Quality practice parameters are being defined. Board certification in neurocritical care is more common. Nonetheless, education needs continue to be in high demand.

The book is intentionally limited in depth, but comprehensive in scope. The emphasis has been placed on discussing day-to-day management issues that are commonly seen in the neurocritical care unit addressing both medical and neuro-specific management issues.

Upon completion of this book, the reader should be able to understand the nuances in neurocritical care patients and determine the most effective therapy to limit secondary brain injury.

I would like to express my deepest gratitude to the authors, neurocritical nurses and fellows, families, and particularly the patients who continue to stimulate my passion for neurocritical care.

Chapter 1

The Neurological Assessment of the Critically Ill Patient

Abdo Barakat and Diana Greene-Chandos

Critically ill patients admitted to the intensive care unit (ICU) may exhibit signs and symptoms of primary or secondary neurological disorders. Factors such as altered mental status, agitation, pain, sedation, neuromuscular blockade, hypothermia, metabolic disturbances, intubation/mechanical ventilation, and surgical or traumatic lesions of the extremities may complicate the interpretation of the neurological assessment in the ICU. Nevertheless, neurological signs in the critically ill have been established as prognostic indicators and markers of severity. Subsequently, a proper neurological assessment of the critically ill patient remains a central aspect of care, diagnosis, and prognosis [1].

General Approach to the Neurological Assessment

1. *History*: Obtaining a history from the patient, family, friends, or witnesses is invaluable. Investigate the context of the presenting illness, the chronological sequence of events, any past medical history, medications, or allergies.
2. *General medical exam*: A general medical exam and assessment of vital signs should always precede the neurological exam.
3. *Level of consciousness*: The level of consciousness can be described using three parameters: awake, alert, and aware. Albeit simplistic, this approach is a valid method of evaluating the level of consciousness, and subsequently guiding the neurological exam. Table 1.1 offers definitions of various states of altered consciousness.
   - Conscious patient:
     - Proceed with the traditional neurological examination including cognition, cranial nerves, motor and sensory function, reflexes, and coordination.
     - Adapt the exam to the underlying neurological process [1].
     - Serial examinations offer insight into potential trends of improvement or worsening [1].
   - Sedated patient:
     - Assess the feasibility of interrupting sedation.
     - Score delirium, coma, and muscular strength using validated scales following interruption[1,2,3].
   - Comatose patient:
     - Assess the level of arousal, brainstem function, motor responses, and respiratory pattern [2].
     - This can be achieved by means of validated scoring systems, mainly the Glasgow Coma Scale (GCS) [4] or the Full Outline of UnResponsiveness (FOUR) scale [5] (Table 1.2).
4. Every patient admitted to the ICU should receive a baseline neurological assessment, followed by serial exams on a daily basis at a minimum. A higher frequency can be tailored to the individual needs of every critically ill patient [1].

Sedation

Sedation can mask certain neurological signs of progression or deterioration towards life-threatening events, especially in patients with primary neurological injury [6]. Accordingly, continued sedation is not only a potential confounding factor in the neurological assessment, but also a risk for missing certain neurological complications of other systemic diseases such as ischemia, leukoencephalopathy, or hemorrhage secondary to septic shock[7,8]. Moreover, sedation was found to be an independently modifiable risk factor in terms of time-to-extubation and mortality [8]. Studies have shown that in the case of mechanically ventilated patients, routine interruption of continuous sedation (ICS) is recommended and leads to reductions in the amount of time spent in the ICU and in the risk of developing complications secondary to prolonged mechanical ventilation[1,8,9–11].

Critically ill patients with elevated intracranial pressure (ICP) are the exception to the above recommendation, and routine ICS should be deferred [1]. Nevertheless, a focused neurological exam could still offer meaningful information, as brainstem reflexes can still be assessed in the context of sedation and any abnormalities carry prognostic significance [12].

Delirium

Delirious states can be commonly found in patients suffering from diffuse toxic, metabolic, or multifocal injuries to the central nervous system[2]. Its manifestations are the result

Table 1.1 States of altered consciousness

States of acutely altered consciousness	States of subacute or chronic alterations in consciousness
Clouding of consciousness: a state with reduced wakefulness, awareness, or attention	Dementia: not accompanied by reduction in arousal
Delirium: a floridly abnormal mental state characterized by disorientation, fear, irritability, misperception of sensory stimuli, and often, visual hallucinations	Hypersomnia; a state characterized by excessive but normal-appearing sleep from which the subject readily, even if briefly, awakens when stimulated
Obtundation: a state of mental blunting and torpidity, characterized by reduction in alertness, slower psychological responses to stimulation, and increased sleep time	Vegetative state: a return of wakefulness after severe brain injury accompanied by an apparent total lack of cognitive function
Stupor: a condition of deep sleep or behaviorally similar unresponsiveness from which the subject can be aroused only by vigorous stimuli	Brain death: a state in which all functions of the brain, including cortical, subcortical, and brainstem functions, are permanently lost
Coma: a state of unarousable unresponsiveness in which the subject lies with eyes closed	Others; akinetic mutism, apallic syndrome, locked-in syndrome

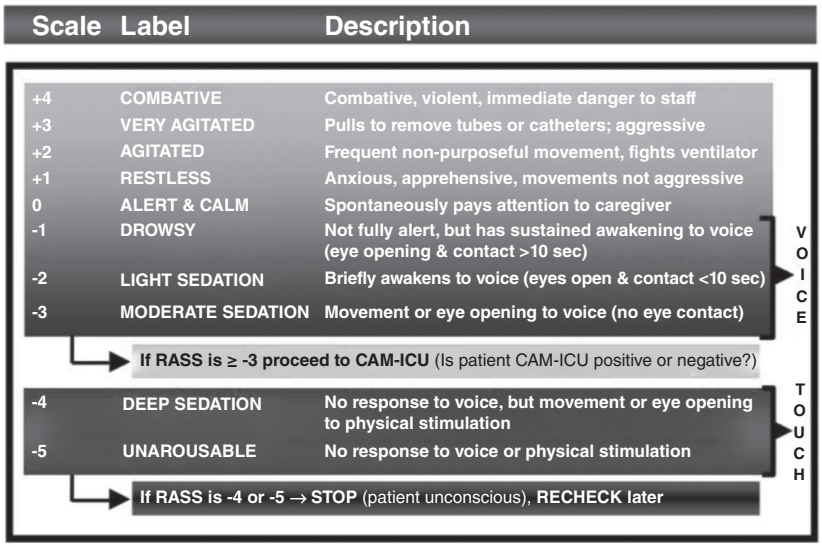
Adapted from reference [2].

Table 1.2 Glasgow Coma Scale (GCS) and Full Outline of UnResponsiveness (FOUR) scores

	Glasgow Coma Scale	FOUR score
Eye response	4 = eyes open spontaneously 3 = eyes opening to verbal command 2 = eyes opening to pain 1 = no eyes opening	4 = eyelids open or opened, tracking, or blinking to command 3 = eyelids open but not tracking 2 = eyelids closed but open to loud voice 1 = eyelids closed but open to pain 0 = eyelids remain closed with pain
Motor response	6 = obeys commands 5 = localizing pain 4 = withdrawal from pain 3 = flexion response to pain 2 = extension response to pain 1 = no motor response	4 = thumbs-up, fist, or peace sign 3 = localizing to pain 2 = flexion response to pain 1 = extension response to pain 0 = no response to pain or generalized myoclonus status
Verbal response	5 = oriented 4 = confused 3 = inappropriate words 2 = incomprehensible sounds 1 = no verbal response	
Brainstem reflexes		4 = pupil and corneal reflexes present 3 = one pupil wide and fixed 2 = pupil or corneal reflexes absent 1 = pupil and corneal reflexes absent 0 = absent pupil, corneal and cough reflex
Respiration		4 = not intubated, regular breathing pattern 3 = not intubated, Cheyne–Stokes breathing pattern 2 = not intubated, irregular breathing 1 = breathes above ventilator rate 0 = breathes at ventilator rate or apnea
Max–min	15–3	16–0

of depression in overall brain functioning or bilateral involvement of the limbic structures [2]. Delirium is associated with a number of risk factors, as well as certain outcomes that make its timely diagnosis clinically important.

Delirium is a common problem in the intensive care unit (ICU). Accurate diagnosis is limited by the difficulty of communicating with mechanically ventilated patients [13]. Nevertheless, a number of studies have shown



Sessler, et al., Am J Repir Crit Care Med 2002, 166: 1338-1344 Ely, et al., JAMA 2003; 286. 2983-2991

Figure 1.1 Richmond Agitation-Sedation Scale (RASS) (reproduced with permission).

CAM-ICU Worksheet

Feature 1: Acute Onset or Fluctuating Course	Score	Check here if Present
Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/SAS), GCS, or previous delirium assessment?	Either question Yes →	☐
Feature 2: Inattention		
Letters Attention Test (See training manual for alternate **Pictures**) Directions: Say to the patient, "*I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand*." Read letters from the following letter list in a normal tone 3 seconds apart. **S A V E A H A A R T or C A S A B L A N C A or A B A D B A D A A Y** **Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."**	Number of Errors >2 →	☐
Feature 3: Altered Level of Consciousness		
Present if the Actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4: Disorganized Thinking		
Yes/No Questions (See training manual for alternate set of questions) 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question.** **Command** Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) *If the patient is unable to move both arms, for 2nd part of command ask patient to "Add one more finger" **An error is counted if patient is unable to complete the entire command.**	Combined number of errors >1→	☐

Overall CAM-ICU		
Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive	**Criteria Met →**	☐ **CAM-ICU Positive** (Delirium Present)
	Criteria Not Met →	☐ **CAM-ICU Negative** (No Delirium)

Figure 1.2 CAM-ICU worksheet (reproduced with permission).

that an accurate diagnosis is still feasible in the ICU setting [13,14]

Recent clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit recommend that all adult ICU patients be regularly assessed for delirium using either the Confusion Assessment method for the ICU (CAM-ICU) or the Intensive Care Delirium Screening Checklist (ICDSC) [14]. It is recommended to

assess for delirium at repeated intervals in order to improve diagnostic sensitivity and monitor response to interventions [1]. The suggested assessment includes two steps:

- Step 1: Sedation assessment using the Richmond Agitation-Sedation Scale [15] (Figure 1.1)
- Step 2: Delirium assessment using the CAM-ICU [13] or the ICDSC [16]. Delirium should only be assessed after the interruption of sedation in order to distinguish it from persistent sedation [16] (Figure 1.2).

Stupor and Coma

Assessing a critically ill patient with impaired consciousness is no simple feat. Stupor and coma can be manifestations of a wide array of disturbances, and a systematic approach to assessment and diagnosis is crucial, especially in the case of reversible causes [17]. To note, the priority before obtaining any answers is to evaluate for and secure neuro-protection by stabilizing the patient [2,17]. The pathophysiology of impaired consciousness can be divided into two broad mechanisms [2,18]:

1. Depressed functioning of the cerebral hemispheres (+/– some brainstem structures); diffuse bilateral hemisphere damage
2. Injury to brainstem (reticular) activating mechanisms.

These mechanisms can alternatively be explained by disturbances that either cause structural brain lesions or diffuse neuronal dysfunction [17]. A rare group of conditions can mimic coma, such as psychogenic unresponsiveness secondary to catatonia or conversion reactions [2]. Those conditions still deserve a full medical and neurological assessment to rule out the presence of a structural or organic disturbance that might present with psychogenic features. For instance, a bilateral thalamic stroke can be misdiagnosed as a conversion reaction [17].

Assessing a Patient with Impaired Consciousness

A structured and systematic approach to the assessment of a comatose patient (or any patient with impaired consciousness) can prove useful.

1. Initial Stabilization

The initial stabilization of a critically ill patient presenting with impaired consciousness should be the primary objective of the ICU team. Patient stabilization includes the following [2,17,19]:

- Ensuring patent airways
- Supporting breathing and ventilation (oxygen saturation $\geq$96%)
- Aspiration prevention
- Maintaining circulation: IV access, blood pressure management
- Drawing blood for analysis and cultures (if febrile)
- Immobilizing the cervical spine until it is cleared
- Empiric treatment for infection if suspected on admission
- Lowering intracranial pressure: elevate the head of the bed to 30° if increasing ICP; flatten it if suspecting a posterior circulation stroke
- Seizure control if clinically indicated
- Administering thiamine and giving glucose pending lab tests
- Adjusting body temperature
- Restoring acid–base and electrolyte balance
- Considering antidotes if a drug overdose is suspected (routine administration of antidotes is not recommended; supportive care is superior)

2. Initial Assessment

- *History*: Obtain a history from relatives, friends, witnesses, or even law enforcement officials
- *Physical exam*:
  - Vital signs: any abnormality in vital signs is significant to the diagnosis and/or management
  - General physical exam: signs of nuchal rigidity, trauma, acute or chronic systemic illness, drug or poison ingestion [2,17,18]
  - Focused neurological exam (detailed in Section 3. below)
- Laboratory tests and ECG [17,20]. Some initial tests may include some or all of the following depending on the clinical setting [20]:
  - Complete blood count with differential, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)
  - Serum electrolytes, blood urea nitrogen (BUN), creatinine, glucose
  - Thyroid, parathyroid, and adrenal function tests
  - Liver function tests, amylase, lipase, ammonia
  - Troponin levels
  - Arterial blood gases with lactate level
  - Cerebrospinal fluid evaluation, including cytology
  - Body fluid cultures (blood, urine, stool, sputum, CSF)
  - Culture of indwelling catheters
  - Serum and urine toxicology
  - Antiepileptic drug levels
  - Heavy metals.

3. Focused Neurological Exam

Critically ill patients with impaired consciousness have limited to no ability to cooperate with the examiner. Given technological advances, it might be tempting to resort prematurely to neuroimaging or neurophysiologic testing. However, a focused neurological exam remains the cornerstone of the initial assessment, guides the choice of advanced testing, and most importantly, allows the proper interpretation of findings on those more sophisticated tests [18]. In the ICU setting, such an exam aims at localizing the anatomy and depth of coma by unveiling certain lateralizing or focal signs, as well as highlighting any brainstem dysfunction [17].

GCS and FOUR Score

One way to proceed with the examination is to quantify the depth of coma by using validated scoring systems that evaluate some or all of the following: the level of consciousness, motor responses, brainstem function, and respiratory patterns [2].

The Glasgow Coma Scale (GCS) and the Full Outline Of UnResponsiveness (FOUR) score have been the most widely used [4,5]. The GCS has been utilized in intensive care settings for decades. It measures verbal responses, motor responses, and eye opening by scoring the best responses to graded stimuli, with the aim of defining the depth and duration of impaired consciousness and coma [2,4]. Two main limitations to that system are the inability to properly assess intubated or aphasic patients, and the fact that the score does not include a component to score brainstem functioning[5]. The FOUR score was subsequently designed to account for those limitations by incorporating breathing patterns and brainstem testing[5]. The FOUR score also allows further assessment of patients with the lowest GCS score (GCS = 3), and is able to identify locked-in syndrome as well as herniation processes [5,21]. Multiple prospective studies showed that both scores had good overall performance, and both remain valid methods to be used in the ICU [1,20,22]. The added benefit of the FOUR score is its robust predictive value in the prognosis of poor outcome [20].

Table 1.2 illustrates both scoring systems. Documenting the score of every component separately offers added clinical value compared to a total sum of scored components [17].

Respiratory Patterns

An abnormal respiratory status can lead to hypoxemia, acid–base disturbances, and electrolyte imbalances, all of which can contribute to the progression of neurological damage. The breathing pattern can also offer some localizing information, but it has to be interpreted in the context of other signs, as there can be overlap (Table 1.3).

The Eye Exam

- Observe the resting position of the eyes, and note any conjugate or disconjugate deviation (Table 1.4).
- Note any spontaneous eye movements (Table 1.5)
- Inspect both pupils in terms of size, shape, and symmetry. Note the presence of anisocoria, if any (i.e. difference in pupil size >1 mm).
- Perform a fundoscopy to assess for subhyaloid hemorrhages, hypertensive retinopathy, and papilledema [17,18]. The absence of papilledema does not rule out elevated ICP [18]. The presence of venous pulsations is characteristic of a normal ICP, but their absence is less meaningful [17].
- Ocular ultrasonography of the optic nerve sheath with a high-frequency probe can offer accurate measurement of ICP when fundoscopy is not revealing, but suspicion is high [17].

Brainstem Reflexes

Brainstem reflexes not only help localize lesions, but also help guide the need for supportive care in the critically ill patient. Compared to abnormal motor responses, brainstem reflexes are more useful in localization as they can be traced back to the location of the cranial nerve nuclei involved [17] (Table 1.6). Of note, abnormal brainstem reflexes need not solely arise from intrinsic brainstem pathologies, but also from extrinsic processes exerting a mass effect on the brainstem, as in the case of herniation syndromes[17]. The main reflexes discussed in this section are: pupillary responses, eyelid and corneal reflexes, oculocephalic and oculovestibular reflexes, and gag and cough reflexes.

Pupillary Responses – – In addition to inspecting pupil size, shape, and symmetry, pupillary responses (*Afferent: CN II – Efferent: CN III*) should be assessed to evaluate the functioning of CN II and III, the presence of central autonomic disturbances such as Horner's syndrome, and to distinguish structural from metabolic causes [18]. Shine a light into one pupil, and also into the other pupil. Note if the pupils are equally reactive or unreactive, if the response is brisk or sluggish, and if it is consensual (Figure 1.3). Confounding factors that should be noted include: previous ocular injury and recent use of mydriatics or other drugs, such as atropine or dopamine [18].

Eyelid and Corneal Reflexes

- Observe the position of the eyelids. In most cases of impaired consciousness, the eyes will be closed. Open the eyes by lifting the eyelids and release them. A normal response would be a gradual return to baseline position. Failure to close back to baseline on either side points towards an ipsilateral facial nerve dysfunction [2].
- Observe blinking. Spontaneous blinking is suggestive of an intact pontine reticular formation. Unilateral absence of blinking is suggestive of ipsilateral facial nerve dysfunction. The complete absence of blinking points towards a structural or metabolic process affecting the reticular formation [2].
- The corneal reflex (*Afferent: CN V – Efferent: CN VII*) is tested by touching the edge of the eye (not over the iris) with a cotton wisp, a tissue, or other soft material. Brushing the eyelashes or tickling the inside of the nose can also elicit a sensorimotor reflex. The following responses can be observed [2]:
  - Eyelid closure; suggestive of an intact facial nerve and CN VII nucleus
  - Bell's phenomenon; a conjugate upward deviation of the eyes indicating intact brainstem pathways from the CN III nucleus in the midbrain to the CN VII nucleus in the lower pons
  - Contralateral jaw deviation (corneal pterygoid reflex); a phenomenon that may occur when a lesion injures the trigeminal nucleus above the mid-pons. In this case, Bell's phenomenon disappears.

Table 1.3 Respiratory patterns in brain injury [2,17]

	Respiratory pattern		Area of concern
Normal		Patient awake	Small and unilateral lesion
Cheyne–Stokes		Hyperpneic phase lasts longer than the apneic phase	Large bilateral hemispheric; metabolic brain dysfunction
Cheyne–Stokes variant		Shorter apneic phase	Large unilateral injuries
Central neurogenic hyperventilation		Sustained, regular, rapid, fairly deep hyperpnea	Lower midbrain; upper pons; systemic hypoxia; metabolic acidosis; often associated with brainstem tumors
Apneustic		Prolonged inspiratory phase or pauses alternative with expiratory pauses	Bilateral, mid- or lower pons, very poor prognosis
Cluster		Clusters of breath separated by irregular pauses	Lower pons, medulla
Ataxic		Completely irregular, deep breaths, shallow breaths	Medulla; very poor prognosis
Hiccups			Medulla
Sighs or yawns			Rapidly increasing ICP

Oculocephalic Reflex – –The oculocephalic reflex is also known as the doll's head eye phenomenon or the proprioceptive head-turning reflex. The afferent pathway of this test is debated to either arise from the vestibular system or the proprioceptive afferents from the neck [2]. The excitatory stimuli to the extraocular muscles appear to travel via the medial longitudinal fasciculus [2]. Before performing this maneuver, ascertain that the cervical spine is cleared [2,18]. To perform this maneuver, keep the eyelids open and briskly turn the patient's head from side to side with a brief pause at endpoints [2]. In a comatose patient with intact brainstem and cranial nerves, the normal response is a contraversive conjugate eye deviation [2,18]. This means that the eyes turn to the left, laterally, when the head is turned to the right. Flexing and extending the neck can be performed as well [2]. Similarly, a normal response would be a conjugate upward eye deviation with neck flexion. An absent oculocephalic reflex means that the eyes follow the head movement [2].

Table 1.4 Eye deviation corresponding to brain injury [17,18]

Conjugate deviation	
Frontal lobe	Eyes look towards the lesion
Medial thalamus, pons, seizures	Eyes look away from the lesion or focus
Thalamus, midbrain pretectum, or metabolic causes	Downward deviation
Brainstem, sleep, seizures	Upward deviation
Disconjugate deviation	
(Right) CN III palsy	(Right) Eye "down and out," (Right) pupil dilated
(Right) CN VI palsy	(Right) Eye inwardly deviated
Posterior fossa	Skew deviation, vertical displacement

Oculovestibular (Caloric) Reflex

- Oculovestibular testing affects similar pathways to those involved in the oculocephalic reflex. The test utilizes a stronger stimulus, calorics, to stimulate convection currents in the endolymph, which in turn activate vestibular receptors and subsequently eye deviation [2]. Before the test is done, use an otoscope to ensure that the ear canal and tympanic membrane are intact [2,17].
- Cold-water calorics: Slowly infuse water, 50 cm^3 at 30 °C or 1 cm^3 of ice water, into the ear canal using a syringe, with the head of the bed elevated at 30° [2,17].
  - In a conscious patient, ice-cold water into the right ear, for example, induces nystagmus with the slow component towards the right (the irrigated ear) and the fast component contralaterally [2]. This can also be observed in psychogenic coma [17].

Table 1.5 Spontaneous eye movements in unresponsive patients [2,18]

Purposeful eye movements	Consider locked-in syndrome, catatonic, pseudo-coma
Roving eye movements (slow, conjugate)	Nonspecific (toxic, metabolic, bilateral hemispheric); CN III and VI intact
Nystagmus: 1. Spontaneous nystagmus 2. Refractory nystagmus (irregular jerks of the eyes backward into the orbit) 3. Convergence nystagmus (slow divergent phase, quick convergent phase) 4. Nystagmoid jerking of a single eye	1. Uncommon in coma; consider pseudo-coma 2. Mesencephalic tegmental lesions 3. Mesencephalic lesions 4. Severe mid-pontine to lower pontine damage
Ocular bobbing (rapid conjugate downward movement, slow recovery to mid-position)	Acute pontine lesions

Table 1.6 Neurological findings that help to localize site of structural brain disease by location of lesion

Cortical	Variable motor response Spontaneous eye movements (roving, dipping) Upward or downward eye movement
Brainstem	Anisocoria Mid-position fixed pupil Occupation bobbing Skew deviation Internuclear opthalmoplegia Extensor or flexor posturing

- In a comatose patient, the eyes should tonically deviate towards the side of cold irrigation if the brainstem is intact [17]. Limited irregular beats of nystagmus may be observed initially, but the eyes should ultimately and tonically deviate towards the irrigated side for up to 2–3 minutes. Therefore, hold off for 5 minutes before testing the opposite ear [2].
- To test for vertical eye movements, both canals have to be irrigated simultaneously with ice water. In a comatose patient, a normal response involves downward gaze [2].
- The absence of response should be interpreted with caution as this may be the result of various etiologies, such as brain death, brainstem lesions, pre-existing vestibular disease, ototoxic drugs such as gentamicin, vestibulosuppressant drugs such as sedatives, phenytoin, or tricyclic antidepressants, neuromuscular blockade, and other metabolic causes.

- Warm-water calorics: The same sequence as described above can be performed by irrigating with warm water, no more than 44 °C [2].
  - In a comatose patient with an intact brainstem, the eyes should tonically deviate away from the irrigated ear [2].
  - To test for vertical eye movements, both canals have to be irrigated simultaneously with warm water. A normal response involves an upward gaze [2].

Gag and Cough Reflexes – – CN IX constitutes the afferent component of both gag and cough reflexes, while CN X constitutes its efferent component. Both their nuclei are located in the medulla, a part of the brainstem not well tested by scoring systems such as the GCS or the FOUR score [24]. Testing both reflexes is relatively easy to do. It allows the examiner to assess the integrity of the lower brainstem, and also guide airway protection and mechanical ventilation protocols in patients with impaired gag or cough reflexes [24].

Neurocritical care patients on mechanical ventilation are at high risk of developing acute lung injury, and the absence of either gag or cough reflexes is strongly predictive of that [24]. Patients receiving neuromuscular blockers or therapeutic overdose of sedatives may have absent gag and cough reflexes, and therefore the examiner should always be aware of pitfalls in the interpretation of findings [2].

- The pharyngeal or gag reflex: If a patient is not intubated, test by stimulating the posterior pharynx with a tongue depressor, a cotton swab, or suction device [25]. The gag reflex is more difficult to test for in an intubated patient. If such a situation, jiggle the endotracheal (ET) tube gently back and forth, and observe for a response. The gag reflex may be suppressed in patients who have been intubated for a while, and consequently, testing the cough reflex is of value [26].
- The tracheal or cough reflex: This test is performed by advancing a suctioning catheter into the ET tube down to the level of the carina [25]. A cough response should be elicited following one or two suctioning passes if the medulla is intact [25].

Motor Responses

The goal is to be able to assess motor function in the setting of impaired consciousness. Motor responses are thus evaluated by observation and graded stimuli. Spontaneous movements or posturing should be noted [17]. The nature of responses to further verbal and noxious stimuli can help localize the anatomy of the brain insult [18,19].

Stimuli should be administered on both sides of the body to assess for asymmetry. Noxious stimuli elicit pain, but should not cause injury [18]. This can be done by applying pressure over the supraorbital ridge or the temporomandibular joint, rubbing the sternum, compressing the nail bed, or pinching the Achilles tendon [17,18]. A normal response would be to fend off the examiner's hand or at least localizing where the pain is coming from. The other thing to observe is the presence or absence of a cortico-sensory response [27]. Grimacing of the face is such a cortical response [27], and may be present in the absence of limb movements [18].

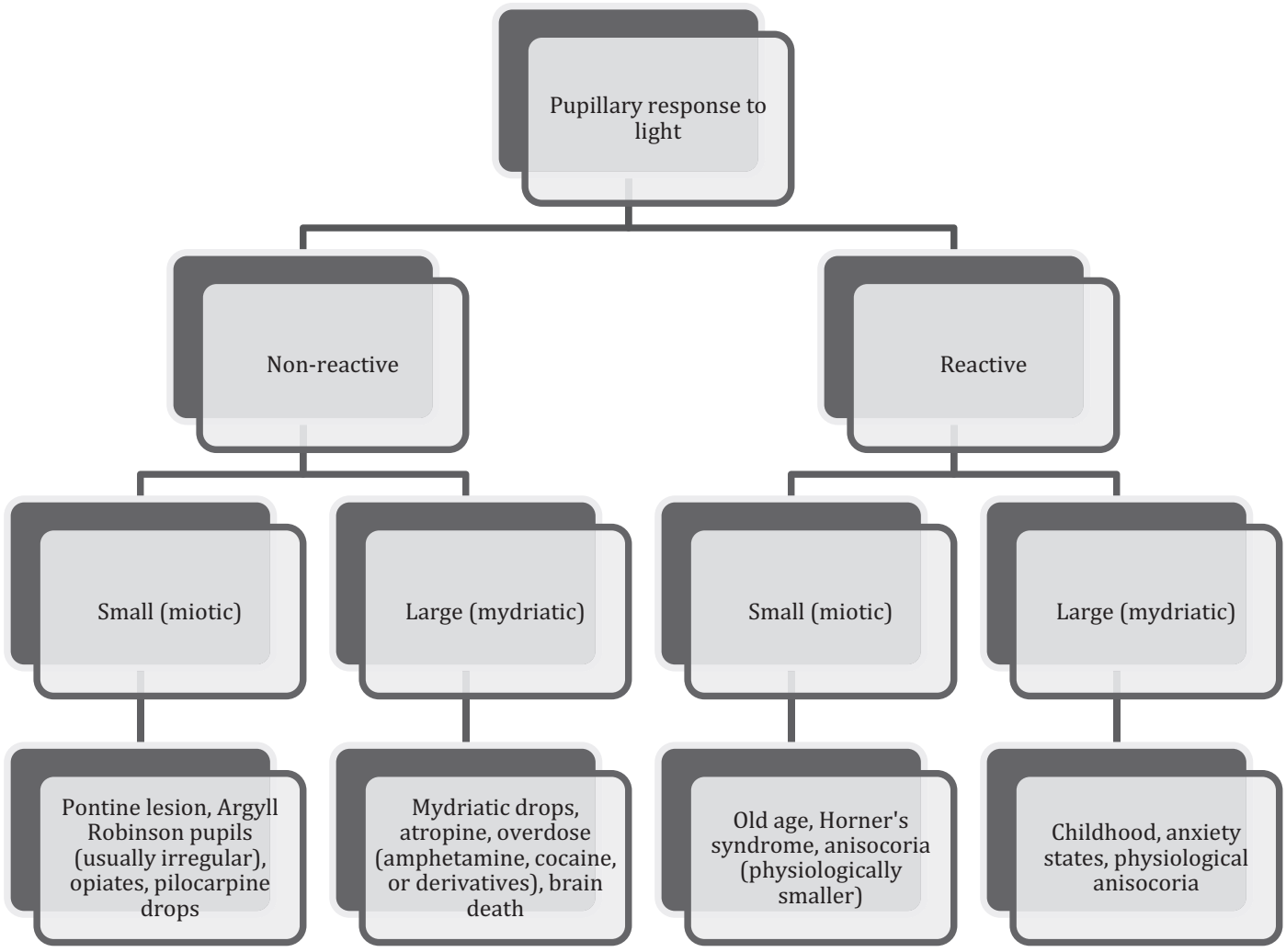


Figure 1.3 Pupillary abnormalities (adapted from reference [23])

- A patient with a diffuse metabolic encephalopathy might withdraw away from the stimulus, and this response may be asymmetric if one hemisphere is affected more than the other [28].
- When the insult affects the upper midbrain, the motor response to noxious stimuli may translate into decorticate posturing, which can be unilateral or bilateral depending on the anatomy of the lesion: arms are flexed, legs are extended, and toes extend downward [18,28].
- When the insult affects the lower midbrain or upper pons, the motor response to noxious stimuli may translate into decerebrate posturing: arms, legs, and toes are extended [28]. Decerebrate rigidity describes a bilateral process, whereas a decerebrate posture describes a unilateral process [18].
- When the insult affects anywhere along the medullopontine reticular formation or the acute motor phase of a spinal cord transection, the motor response is either flaccid or absent [2].

Assessing Neuromuscular Complications

- Patients admitted to the ICU may have motor weakness that is pre-existing or undiagnosed, newly acquired, or associated with their critical illness [29,30].
- Nevertheless, the complexity of the intensive care setting poses limitations on the assessment and diagnosis of motor weakness. Patients may be sedated, noncooperative, or unable to communicate, which makes the performance and interpretation of the neurological exam challenging [29]. Accordingly, the primary step to approach a case of motor weakness is understanding its clinical setting by investigating the patient's history and charts, list of medications received in the ICU, and precipitating factors, such as electrolyte disturbances, drugs, infections, trauma, or prolonged immobility [29].
- The motor exam should be complete and systematic in order to highlight the etiology of weakness. As discussed earlier, consider routine interruption of continuous

sedation in order to limit its confounding effects on the exam, and to increase the chance of patient cooperation [31].
- In the presence of fixed or focal signs, or impaired consciousness despite the interruption of sedation, neuroimaging and/or neurophysiologic testing should be considered [31].
- The motor exam should help distinguish the various etiologies of weakness [29]:
  - Central nervous lesions
  - Spinal cord lesions
  - Neuromuscular disorders
  - Neuropathic causes of weakness such as compression/entrapment neuropathies, critical illness polyneuropathy (CIP), Guillain–Barré syndrome, etc.
  - Myopathic causes of weakness such as critical illness myopathy (CIM) or rhabdomyolysis.
- ICU-acquired weakness (ICU-AW) is a potential complication of critical illness that should be investigated in a patient presenting with diffuse symmetrical weakness, respiratory muscle weakness, and facial muscle sparing [32].
  - This complication is largely explained by CIP or CIM [32].
  - The neurological exam helps distinguish ICU-AW from other neuromuscular disturbances. In ICU-AW, upper motor neuron signs are absent, facial and extraocular muscles are spared, weakness is symmetric and diffuse, and it does not fluctuate or progress in ascending or descending patterns [1,32].
- The following features should be noted on the motor exam[2,23]:
  - Symmetry in every aspect of the exam
  - Facial or extraocular muscle involvement
  - Proximal or distal muscle involvement
  - Respiratory muscle involvement
  - Progression of muscle weakness: rapid, slow, fluctuating, ascending, descending
  - Muscle tone: normal, rigid, spastic, paratonic, hypotonic, flaccid
  - Deep tendon reflexes: increased, normal, decreased, or absent
  - Superficial and plantar reflexes
  - Muscle atrophy
  - Other motor signs such as fasciculation, fatigability, or myalgia
  - Other neurological signs such as dysautonomia or sensory loss.

Conclusion

The take home message of this chapter revolves around five recommendations with regards to the neurological assessment of the critically ill [1]:

(1) Every critically ill patient in the ICU should receive a proper neurological assessment.
(2) Every neurological assessment should evaluate consciousness and cognition, brainstem function, and motor function. The level of consciousness guides the subsequent exam.
(3) The confounding effect of sedation on the interpretation of the neurological assessment should be managed by interrupting sedation, unless the risks of interruption outweigh the benefits of minimizing the confounding potential, such as in patients with reduced intracranial compliance.
(4) The neurological assessment should precede and guide any subsequent testing or imaging.
(5) Certain aspects of the neurological assessment carry a prognostic significance in well-defined patient populations, and should help guide goals of care.

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Chapter 2

Cerebral Blood Flow Physiology and Metabolism in the Neurocritical Care Unit

Rajat Dhar and Michael Diringer

The brain has high energy requirements combined with an inability to store substrates critical for this tissue metabolism. This precarious balance results in a vital organ that is highly dependent on constant blood flow, providing oxygen and glucose via tissue perfusion. Although the brain only comprises 2% of total body weight, it receives 15% of cardiac output (700 ml/min) at rest, and accounts for 20% of oxygen consumption, and an even greater proportion of glucose utilization. Even brief interruptions in blood flow can trigger acute cerebral dysfunction, whether loss of consciousness from global hypoperfusion (e.g. syncope from non-perfusing cardiac arrhythmias or hypotension) or focal neurological deficits relating to ischemia from thromboembolism or vasospasm.

Normal Physiology of Cerebral Blood Flow

Cerebral blood flow (CBF) is the primary measure of brain perfusion, and thus serves as a vital parameter in assessing the adequacy of substrate delivery and viability of brain tissues. It is expressed in volume of blood reaching a defined mass of brain tissue in a given time period (typically ml/100 g/minute). Normal CBF is approx. 50 ml/100 g/min, but may decrease slightly with age [1]. This whole-brain value averages more metabolically active gray matter (70–80 ml/100 g/min) and the white matter (20 ml/100 g/min). Flow must be adequate to deliver sufficient glucose and oxygen to meet cerebral metabolic demands, primarily required to maintain neuronal ion gradients and support synaptic transmission. To ensure this critical balance in the absence of significant storage capacity, flow and metabolism are usually tightly coupled, whereby increases in metabolism (expressed, for oxygen utilization, as $CMRO_2$, cerebral metabolic rate of oxygen) are matched by increases in CBF and hence greater oxygen delivery (DO_2 = CBF × CaO_2, the arterial oxygen content). Nonetheless, CBF normally delivers 2–3 times the required oxygen (DO_2 approx. 8 ml O_2/100 g/min, compared to a $CMRO_2$ of approx. 3 ml/100 g/min), allowing for some reserve in cases of reduced CBF and/or DO_2. The proportion of oxygen extracted (expressed as OEF, oxygen extraction fraction) remains around 30–35% in normal conditions, rising only if DO_2 falls out of proportion to $CMRO_2$. This is usually due to global or regional hypoperfusion (i.e. reduction in CBF), but can also occur due to arterial desaturation (i.e. systemic hypoxemia) or anemia. The Fick principle describes the relationship between metabolism, delivery, and extraction of oxygen:

$$CMRO_2 = DO_2 \times OEF = CBF \times AVDO_2$$

(arteriovenous difference in oxygen content)

Autoregulation

Given the importance of perfusion to neuronal function and integrity, homeostatic mechanisms actively maintain stable and adequate levels of CBF in the face of physiologic perturbations, largely through adaptive vascular reactivity. A fundamental instance of this is the ability of the brain to regulate its own perfusion, independent of changes in systemic blood pressure and cardiac output, a process termed cerebral pressure autoregulation. As systemic and hence cerebral perfusion pressure changes, cerebral precapillary arterioles respond with changes in tone [2]. The resultant change in vessel diameter impacts flow through these resistance vessels, as governed by the Hagen–Poiseuille law of laminar fluid dynamics, which states that:

$$Q(\text{flow}) = \text{perfusion pressure}/\text{resistance}$$

In the case of cerebral circulation: CBF = CPP/CVR; where cerebrovascular resistance (CVR) is determined by the fourth-power of the vessel radius, and to a lesser extent by blood viscosity. This relationship means that small changes in vessel diameter can result in significant changes in flow. Without pressure autoregulation, a fall in systemic blood pressure and hence cerebral perfusion pressure (CPP = MAP, mean arterial pressure minus ICP, intracranial pressure) would precipitate a potentially dangerous drop in CBF. Instead, resistance vessels increase their diameter in response to lower CPP. This reduction in CVR balances the fall in CPP and maintains constant CBF. However, such vasodilatation will also increase cerebral blood volume (CBV), which, in the setting of reduced intracranial compliance, can increase ICP. Conversely, vasoconstriction protects against hyperemia when CPP is increased, preventing hydrostatic cerebral edema as MAP rises. CBF remains maintained at constant levels despite the vagaries of systemic circulation along this autoregulatory plateau (Figure 2.1).

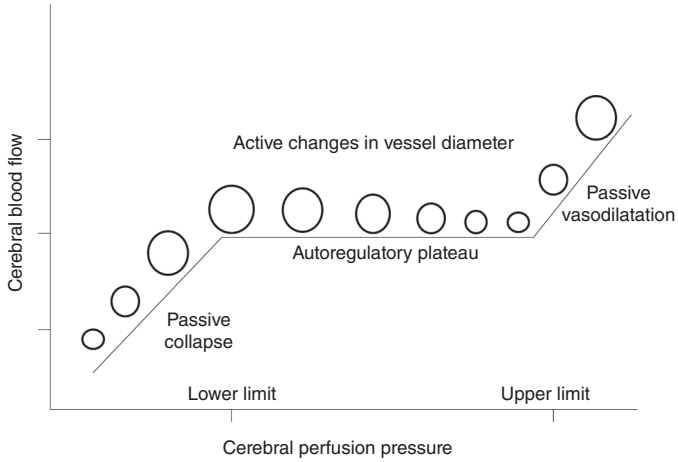

Figure 2.1 Cerebral pressure autoregulation: cerebral blood flow is preserved within limits of autoregulation by changes in vessel diameter.

However, there is a limit to the extent of this autoregulatory compensation. Once a vessel is maximally dilated or constricted (i.e. exhaustion of autoregulatory reserve), further changes in CPP will result in altered CBF. At perfusion pressures beyond these limits (typically below 50–60 mmHg at the lower end and above 150 mmHg at the upper end), CBF will fall or rise in parallel with changes in MAP and CPP. These limits are shifted to the right in patients with chronic, especially untreated, hypertension [3], making such patients more vulnerable to hypoperfusion if blood pressure is lowered even to relatively normal levels. As pressure rises above the upper threshold of autoregulation, CBF will rise, and hypertensive encephalopathy and endothelial damage associated with hydrostatic cerebral edema can occur [4].

Relationship Between CBF and P_aCO_2

The cerebral circulation is not only responsive to changes in pressure, but also to a number of other physiologic parameters. Partial pressure of carbon dioxide (P_aCO_2) is one of the most powerful such modulators. Between P_aCO_2 levels of 20–80 mmHg, a rise of even 1 mmHg can result in an increase in CBF of 3–4% [5]. Such changes in CBF are the result of changes in arteriolar tone, in this case occurring in response to changes in local pH. When P_aCO_2 rises, acidosis causes vasodilatation and higher CBF, while with hyperventilation, P_aCO_2 falls, vessels constrict, and CBF falls. This is the basis by which hyperventilation lowers CBV and thereby can reduce ICP, albeit at the expense of lower CBF and potentially even ischemia in susceptible patients. The onset of this effect is rapid but not durable. pH adapts and normalizes over a few hours, meaning vessel diameter and CBF return to baseline.

Changes in P_aO_2 within the normal range do not affect CBF in the same way. Only when P_aO_2 falls below 50–60 mm Hg, such that arterial desaturation occurs, does the resultant drop in oxygen saturation (SaO_2) and hence artertial oxygen concentration (CaO_2) lead to reduced DO_2 and compensatory vasodilatation; this in turn raises CBF and restores DO_2 to normal levels. A similar homeostatic response occurs in the face of anemia, as lower hemoglobin also reduces CaO_2, resulting in vasodilatation, higher CBF, and restored DO_2 [6]. The effects of reduced blood viscosity at lower hematocrit levels may (through the Hagen–Poiseuille law) further improve CBF in those with anemia.

These regulatory vasomotor responses do not occur in isolation and so are not independent of one another. If vessels are maximally dilated (for example, in response to hypotension or proximal stenosis/occlusion – reducing perfusion pressure), the ability to compensate for reductions in hematocrit or further drops in MAP will be attenuated or lost [7]. The residual ability to respond to such threats and maintain CBF/DO_2 by vasodilatation is captured in the concept of *cerebrovascular reserve*. Degree of reserve can be assessed by response to changes in pH or P_aCO_2 (e.g. administration of acetazolamide, which induces acidemia and should trigger cerebral vasodilatation if reserve is present). This may be an important marker of future stroke risk, as validated in those with carotid stenosis, where stroke risk was highest in those with impaired vasodilatory reserve [8].

Vascular reactivity and the ability to regulate CBF may be impaired in certain disease states, either globally (e.g. after severe head trauma) or regionally (in the territory of acute focal ischemia or vasospasm [9,10]). Similarly, autoregulation may be impaired in the hemisphere ipsilateral to severe carotid stenosis, leading to hyperemia and hyperperfusion syndrome in some patients after revascularization [11]. Conversely, autoregulation appears to be preserved even within the perihematomal region around intracerebral hemorrhage (ICH) [12]. This means that careful reductions in MAP may be tolerated in such patients without inducing a fall in CBF. Conversely, in situations where autoregulation is impaired, CBF will vary passively with perfusion pressure. In this setting, drops in MAP even within the normal range (especially in chronically hypertensive patients) can reduce CBF further [13]; blood pressure may need to be monitored and maintained scrupulously in such patients to avoid worsening or inducing ischemia.

Cerebral Ischemia

Ischemia occurs when flow is inadequate to supply adequate oxygen to support cellular metabolism such that energy failure occurs (i.e. $CMRO_2$ falls). Critical CBF thresholds may vary depending on the metabolic activity of particular regions/tissues (e.g. gray versus white matter), and systemic oxygen content [14]. Severity of ischemia as well as its duration may determine progression to infarction, as does ability to compensate for reduced CBF and DO_2, mediated by cerebrovascular reserve and elevations in OEF. In general, as CBF falls to half its baseline level (approx. 25 ml/100 g/min), electroencephalogram (EEG) activity slows and neurological function may become altered [15]. Protein synthesis may be inhibited at even higher levels [16]. Once CBF falls below 20 ml/100 g/min, electrical