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Critical Care Management of Neurosurgical Patients

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CLINICAL PEARLS

- The predominant aim in managing critically ill neurosurgical patients is to prevent cerebral ischaemia and exacerbation of neurological injury.
- This is achieved by manipulation of a variety of neurophysiological parameters including intracranial pressure (ICP), cerebral perfusion pressure (CPP) and cerebral blood flow (CBF).
- Knowledge of the aforementioned neurophysiological principles is important in understanding the mechanism of action and application of therapeutic interventions in a neuro-critical care setting.
- Initial assessment of the critically ill neurosurgical patient requires a systemic, methodical and reproducible approach to identify, resuscitate and treat life-threatening insults in the most important sequence in which they occur.
- A variety of techniques allow the multi-modal monitoring of critically ill neurosurgical patients allowing individualisation of treatment; trends and variability over a time course provide more useful information than isolated measurements.
- Complications that are general to all neurosurgical patients, and those that are specific to the each neurosurgical pathology should be investigated for an identified in a deteriorating critically ill neurosurgical patient.
- The diagnosis of brain death is important in critically care settings and familiarity with institutional, regional and national guidance is essential.

Understanding concepts pertaining to the management of critically ill neurosurgical patients is vital for optimizing outcomes. The nervous system is vulnerable not only to effects from the initial insult it suffers from a pathologic process (primary brain or spinal cord injury) but also to systemic factors, which exacerbate this primary injury (ie, secondary brain or spinal cord injury). Critically ill neurosurgical patients are managed in dedicated neurocritical care units (NCCUs). This spectrum includes patients admitted in extremis following their initial injury for preoperative optimization and stabilization, patients in the immediate postoperative phase following elective surgery, and any previously stable patient in a ward setting that suffers a neurologic deterioration.

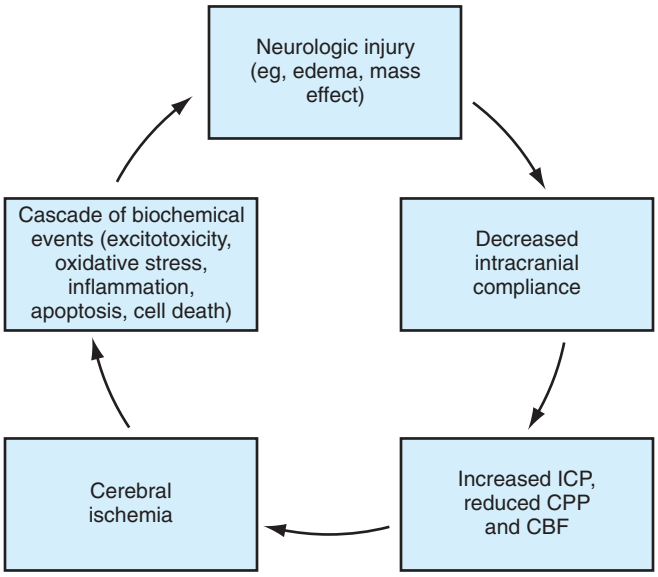
This chapter provides a succinct summary of key concepts regarding the management of critically ill neurosurgical patients including the following:

- Neurophysiologic principles of cerebral homeostasis, cerebrospinal fluid (CSF) flow, cerebral blood flow (CBF) and cerebral perfusion pressure (CPP), intracranial pressure (ICP), and cerebral ischemia and its pathophysiologic impact on the nervous system
- Initial assessment of and etiologies of deterioration in critically ill neurosurgical patients
- Basic concepts of management in NCCUs
- Principles of neurologic monitoring including ICP, jugular venous oxygen saturation ($SjvO_2$), brain tissue oxygen tension ($PbtO_2$), and transcranial Doppler (TCD) sonography
- Specifics of general care in critically ill neurosurgical patients including management of raised ICP, seizures, infection, and electrolyte derangements
- Special considerations on critical care management of neurosurgical pathologies including traumatic brain injury (TBI), vascular pathology (aneurysmal subarachnoid hemorrhage [aSAH], arteriovenous malformations [AVMs], intracranial hemorrhage), brain tumors, posterior fossa surgery, neuromodulation and epilepsy, pituitary surgery, and spinal cord injury
- Concepts regarding diagnosis of brain death

It is beyond the scope of this single chapter to comprehensively cover all topics to the degree each deserves. The reader is advised to refer to the variety of excellent monographs and texts on the subject where necessary.[1,2]

Cerebral Homeostasis

The most significant complication of the majority of neurosurgical pathologies is cerebral ischemia. It is a by-product of a propagating vicious cycle starting with the initial neurologic



• **Figure 26.1** Cerebral ischemia—the end product of a consistently propagating vicious cycle following an initial neurologic injury. *CBF,* cerebral blood flow; *CPP,* cerebral perfusion pressure; *ICP,* intracranial pressure.

injury leading to a reduction in intracranial compliance with increasing ICP and a reduction in CPP and CBF with the resultant ischemic injury exacerbating the neurologic injury (Fig. 26.1).

The predominant aim of NCCU management in critically ill neurosurgical patients is to optimize systemic physiology, contribute to neuroprotection, and control ICP to allow restoration of CPP and CBF, thereby preventing ischemia and limiting secondary brain or spinal cord injury. Understanding the manipulation of the aforementioned parameters requires a brief discussion of the relevant neurophysiologic concepts underpinning CSF production and flow, CBF, CPP, and ICP.

Cerebrospinal Fluid Production and Flow

CSF production is approximately 450 to 500 mL/24 hours and predominantly via three sources: 60% to 70% by choroid plexus (within the lateral, third, and fourth ventricles) with the remaining 30% being extrachoroidal (ventricular ependymal lining, dural lining of spinal nerve roots, brain parenchyma). Absorption is via arachnoid granulations and villi into dural venous sinuses and is dependent on venous pressure. The balance between production and absorption may be altered in pathologic states necessitating CSF diversion to prevent alterations in ICP. Pharmacologic agents such as furosemide (impacts on chloride transport) and acetazolamide (inhibition of carbonic anhydrase) can reduce CSF production.

Cerebral Blood Flow, Metabolism, and Mechanisms of Control

Despite its relatively small size (~2% of total body mass), the brain has the highest metabolic requirement of any organ, necessitating a consistent and reliable blood flow to provide continuously high levels of oxygen delivery and energy substrates (predominantly glucose). It consumes the following:

- 15% of the resting cardiac output (CO) with an average CBF of 750 mL/min
- 20% of the basal oxygen consumption with an average of 50 mL/min
- 25% of the basal glucose consumption

CBF is directly proportional to the CPP and inversely proportional to the cerebrovascular resistance (CVR) of the intracranial vessels:

$$CBF = CPP/CVR$$

The CVR is predominantly a factor of the vessel diameter, which is regulated by smooth muscle contractility in vessel walls: smooth muscle contraction causes vasoconstriction, which decreases vessel diameter with a resultant increase in CVR and vice versa. The CPP is directly related to the mean arterial pressure (MAP) and the ICP via the following equation:

$$CPP = MAP - ICP$$

CBF is regulated by a variety of factors including the following[3]:

- Metabolic demand (including neurogenic and metabolic factors)
- Autoregulation (mediated by neurogenic and myogenic mechanisms)
- Arterial carbon dioxide tension ($PaCO_2$) and oxygen tension (PaO_2)

Flow-Metabolism Coupling

CBF is regionally variable, and the distribution parallels and reflects the degree of metabolic activity in different parts of the brain *(flow-metabolism coupling)*. The average CBF is 50 mL/100 g of tissue/min with areas of increased neuronal activity having a higher cerebral metabolic rate and therefore increased regional CBF (average in gray matter, 80–110 mL/100 g of tissue/min; average in white matter, 25 mL/100 g of tissue/min).

Metabolic activity is reflected by the cerebral metabolic rate of oxygen consumption ($CMR\ O_2$) and the cerebral metabolic rate of glucose utilization ($CMR_{Glucose}$). The close matching of flow metabolism means that although there is regional variation in CBF, $CMR\ O_2$, and $CMR_{Glucose}$, the overall oxygen extraction fraction (OEF) remains relatively constant (~40%). The regulatory changes in flow-metabolism coupling have a short latency (~1 sec) and are mediated by regional metabolic and neurogenic factors.

Metabolic factors exert their effect via a negative feedback mechanism. The initially increased metabolic activity increases the level of local metabolic factors precipitating an increase in perfusion and CBF. This leads to an increased washout of these factors with an associated reduction in flow. Examples of vasodilatory factors (which increase flow) include nitric oxide (NO), specific prostaglandins (PgE_2 and PgI_2), and adenosine. The local levels of these factors may also increase with increased

activity during "stress" states (eg, hypoxia, hypotension, seizures). Vasoconstrictive factors (which decrease flow) include free calcium ion, thromboxane (TxA_2), and endothelin.

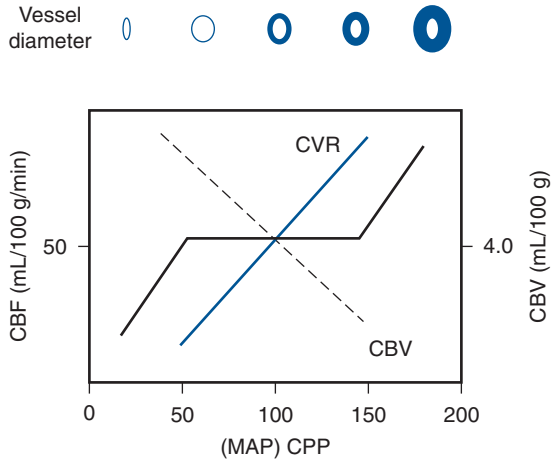
Neurogenic mechanisms work via a combination of sympathetic activity (α-2 adrenergic activity is vasoconstrictive, and β-1 adrenergic activity is vasodilatory) and local neural factors (eg, acetylcholine [ACh], NO, serotonin [5-HT], dopamine [DA], substance P, neuropeptide Y).

Depression of cerebral function (eg, anesthesia, hypothermia, sedation) all suppress metabolism ($CMR\ O_2$, $CMR_{Glucose}$) with a coupled reduction in CBF, whereas hyperthermia and seizure activity increase metabolism and CBF. It is estimated that for every 1°C change in temperature, the $CMR\ O_2$ and CBF can change by as much as ~5%.

Autoregulation

Autoregulation describes the ability of the cerebral vasculature to maintain a relatively constant CBF despite fluctuations in CPP by regulation of the CVR of intracranial vessels. It works independently of other mechanisms of CBF control such as flow-metabolism coupling and $PaCO_2$ (Fig. 26.2).[4]

Autoregulation works within CPP limits (usually between 50 and 150 mm Hg), although there is significant regional variation in the brain and among individuals. Outside of these limits, however, the CBF is directly dependent on CPP: above 150 mm Hg, an increase in CPP results in increased CBF with forced vasodilatation of cerebral arterioles, increased cerebral blood volume (CBV), ICP, and a resultant disruption of the blood-brain barrier and risk of cerebral edema or hemorrhage; conversely, below 50 mm Hg, a decrease in CPP results in a significant drop in CBF, leading to ischemia.

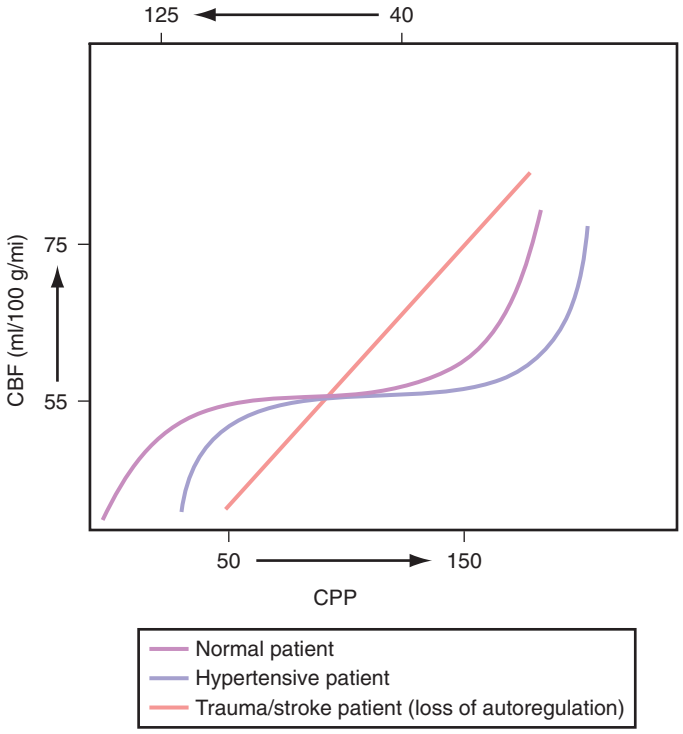


• **Figure 26.2** Autoregulation curve and its impact on CBF. Within the limits of the auto-regulatory plateau, the CBF is kept constant over a range of CPPs (50–150 mm Hg). A decrease in CPP leads to a vasodilation response in vasculature with an increase in vessel diameter. The corresponding decrease in CVR allows an increase in CBV to increase and maintain CBF. The reverse also occurs when CPP increases. *CBF,* cerebral blood flow; *CPP,* cerebral perfusion pressure; *CVR,* cerebrovascular resistance; *MAP,* mean arterial pressure. (From Nortje J. Cerebral blood flow and its control. In: Gupta AK, Gelb AW, eds. *Essentials of Neuroanaesthesia and Neurointensive Care.* Philadelphia: Saunders–Elsevier; 2008: Chapter 3, Figure 3.1.)

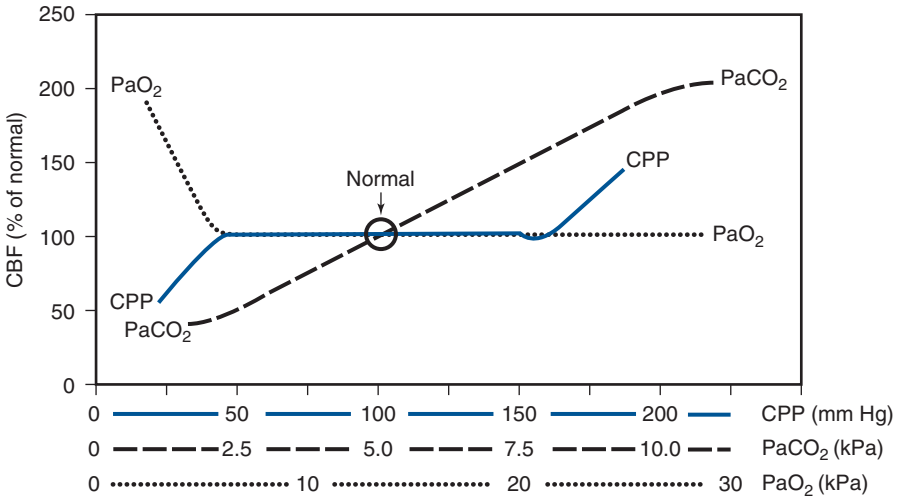
Autoregulation is mediated by myogenic reflexes within the resistance intracranial vessels (predominantly tone and contractility within smooth muscle in arteriole walls) and neurogenic factors (metabolic factors, neural factors, sympathetic activity as described earlier), and these factors are usually slower compared to those of flow-metabolism coupling. Other relevant clinical factors impacting autoregulation include (1) inhalational anesthetics (autoregulation impaired in a dose-dependent fashion), (2) preexisting hypertension (the autoregulation curve is shifted to the right with a narrower plateau and therefore blood pressure required clinically to maintain constant CBF may be higher than expected; targeting lower blood pressures expected with "normal" patients may place the patient in the linear part of the curve with a resultant fall in CBF and ischemic risk), and (3) disruption of the blood-brain barrier in intracranial pathologic processes (eg, trauma, tumors, stroke) where autoregulation is lost (Fig. 26.3).[5]

Impact of $PaCO_2$ and PaO_2

Arterial carbon dioxide tension is a clinically important regulator of CBF; it crosses the blood-brain barrier readily and changes extravascular pH. Increasing $PaCO_2$ (hypercapnia) precipitates vasodilatation with a reduction in CVR and an increase in CBF (up to an upper limit where vasodilatory effects are maximal). Conversely, decreasing $PaCO_2$ (hypocapnia) causes vasoconstriction with increased CVR and decreased



• **Figure 26.3** Impact on autoregulation in pathologic states including patients with preexisting hypertension (the autoregulation curve is shifted to the right with a narrower plateau of autoregulation) and in pathologic states such as trauma, tumors, or stroke patients where the blood-brain barrier disruption results in a loss of the autoregulation responses and the normally sigmoidal shape becomes linear. *CBF,* cerebral blood flow; *CPP,* cerebral perfusion pressure.



• **Figure 26.4** Effect of changes in arterial carbon dioxide tension ($PaCO_2$) and arterial oxygen tension (PaO_2) on cerebral vascular autoregulation and thereby CBF. *CBF,* cerebral blood flow; *CPP,* cerebral perfusion pressure. (From Nortje J. Cerebral blood flow and its control. In: Gupta AK, Gelb AW, eds. *Essentials of Neuroanaesthesia and Neurointensive Care.* Philadelphia: Saunders–Elsevier; 2008: Chapter 3, Figure 3.2.)

CBF and CBV. It is estimated that for 1 mm Hg change in $PaCO_2$ (1 kPa is equivalent to 7.5 mm Hg), the CBF may change by as much as 4% (2 mL/100 g of tissue/min). Clinically in patients with decreased intracranial compliance and therefore raised ICP, hyperventilation-mediated hypocapnia can reduce the CBF, CBV, and therefore ICP.[3]

The manipulation of $PaCO_2$ to control ICP should, however, only be used as a short-term measure until a definitive method of ICP control is instituted. The reasons are twofold: (1) persistent hypocapnia causes vasoconstriction to a maximal limit beyond which tissue hypoxia and cerebral ischemia ensue together with an associated reflex vasodilation, and (2) the effect of decreased $PaCO_2$ is mediated by an increase in the perivascular pH, which is reversed by a corresponding decrease in extracellular fluid bicarbonate to normalize the pH (usually within ~6 hours).

Arterial oxygen tension impacts on CBF but not as significantly as carbon dioxide; CBF is usually unchanged with decreasing PaO_2 until it drops below a threshold (~8 kPa) after which a vasodilatory response is seen. Hyperoxemia may produce some cerebrovascular vasoconstriction, which is postulated to be an evolutionary neuroprotective measure against oxygen free radicals (Fig. 26.4).

Impact of Anesthetic Pharmacologic Agents

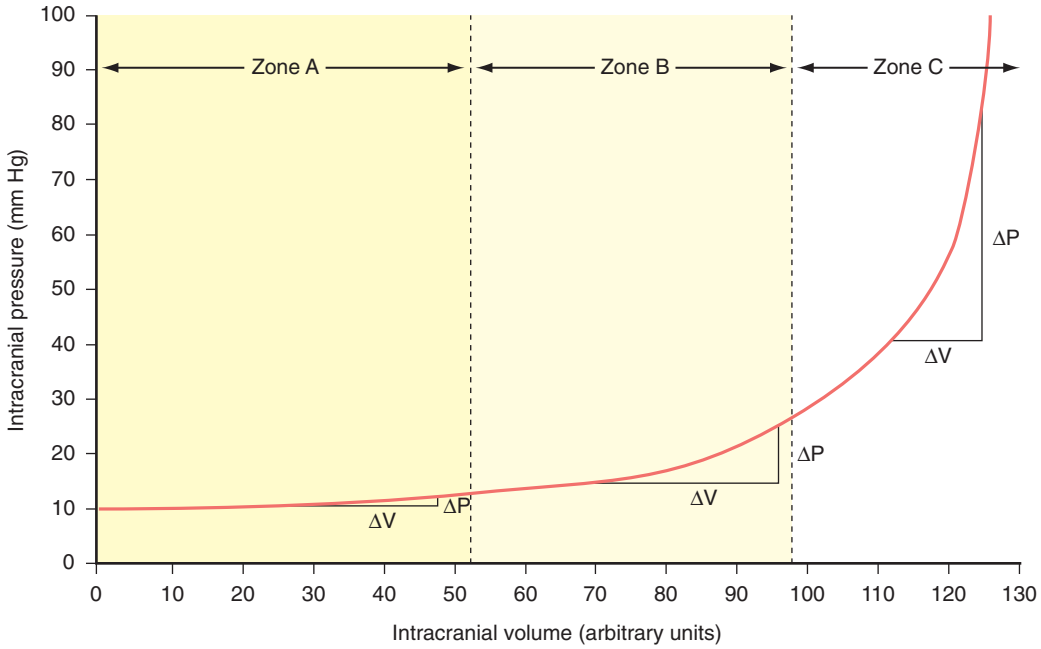
Benzodiazepines and the majority of intravenous (IV) anesthetic agents (eg, etomidate, propofol, thiopental) reduce CMR O_2 and CBF and therefore ICP. This reduction is often in a dose-dependent fashion. Autoregulation, flow-metabolism coupling, and responsiveness to CO_2 remain intact. However, in critically ill neurosurgical patients (eg, traumatic brain injury), flow-metabolism coupling may be impaired and therefore the reduction in CBF (flow) may exceed that of CMR O_2 (metabolism), leading to a mismatch and therefore widened cerebral arteriovenous oxygen gradient and impaired perfusion and ischemia. This must be borne in mind as agents such as propofol—widely used due to a short $t_{1/2}$ allowing rapid emergence if required—may induce precipitous hypotension and a decrease in CPP, especially in hypovolemic patients. Inhalational anesthetics reduce CMR O_2 but increase CBF via a vasodilation effect. Autoregulation is impaired in a dose-dependent fashion. Ketamine increases CMR O_2, CBF, and ICP and therefore is often avoided in critically ill neurosurgical patients.

Intracranial Pressure

ICP is defined as the pressure within the intracranial space relative to atmospheric pressure. Normal ICP may be between 8 and 15 mm Hg, but it is subject to substantial individual variation and physiologic fluctuation (eg, related to posture [supine/standing] and mechanisms such as coughing/straining). The intracranial volume within the intact skull vault is fixed, and the ICP within is dependent on the total volume of contents within the skull.

$$V_{TOTAL} = V_{BRAIN} + V_{BLOOD} + V_{CSF}$$

The brain parenchymal volume takes into consideration extra- and intracellular compartments and contributes ~80% of the total volume (~1400 mL). The blood volume is inclusive of arterial and venous blood and contributes ~10% (~150 mL), whereas the CSF volume also contributes ~10% (~150 mL). The Monro-Kellie doctrine states that an increase in volume of one compartment requires an equal reduction in volume of the other compartments to maintain a constant intracranial pressure within the fixed skull. Of the three compartments the least compressible is the brain parenchyma, whereas the most amenable are the CSF and blood compartments.



• **Figure 26.5** Pressure-volume curve. Zone A: Compensatory and buffering mechanisms (decrease in CSF and venous volumes) are intact and therefore large changes in volume cause little or no change in ICP (ie, low elastance [ΔP/ΔV] with high compliance [ΔV/ΔP]). Zone B: As compensatory measures progressively reduce, the change in ICP for the same change in volume starts to increase (ie, increasing elastance and decreasing compliance). Zone C: Once the threshold for compensatory and buffering capacity has been exceeded (the "decompensation point"), small increase in volume results in a substantial and often exponential increase in ICP (ie, high elastance with low to almost no compliance).

Increased intracranial volume (eg, a space-occupying lesion such as a tumor or hematoma) is initially buffered by displacing intracranial CSF into lumbar cisternal subarachnoid spaces, increasing venous outflow, and reducing CBF and CBV. This initially prevents an increase in ICP. However, there is a limit to which these measures can compensate for increasing intracranial volume. This dynamic relationship is represented by the classical pressure-volume curve (Fig. 26.5). The differential change in pressure per unit volume (ΔP/ΔV) is elastance and its reciprocal is compliance (ΔV/ΔP).[4]

The major complication with persistent and prolonged ICP elevation is twofold: (1) it results in a decrease in CPP (CPP = MAP – ICP) with resultant ischemic injury and (2) it precipitates "shifting" and displacement of cerebral tissue across intracranial compartments with neural tissue compression and devastating complications ("herniation" syndromes; Table 26.1).

Following the introduction of ICP monitoring, and the finding that increased ICP may reduce CBF and that raised ICP (20–25 mm Hg) was associated with poor outcomes, protocol-driven strategies for controlling ICP and CPP in patients with brain injury have become a cornerstone in modern NCCUs.

Cerebral Ischemia

Avoidance of cerebral ischemia is one of the critical aspects in limiting the impact of secondary brain or spinal cord injury. The brain lacks capacity for essential nutrient storage to be used for energy expenditure with minimal reserves of oxygen and energy substrates. The tolerance for reduction in CBF is therefore low.

Pathophysiology

The pathophysiologic processes underpinning ischemia and subsequent infarction are complex and interlinked but broadly speaking involve the following mechanisms: excitotoxicity, tissue acidosis, free radical production, inflammatory cascade activation, cerebral edema, apoptosis, and cell death.[6]

The initial impairment in cerebral perfusion, ischemia, and the resultant lack of adenosine triphosphate (ATP) production results in a failure to maintain normal ionic gradients. Uncontrolled depolarization occurs, followed by the release of excitatory neurotransmitters (glutamate) and calcium. The excitotoxicity exacerbates the depolarization and drives other processes involved in cell necrosis and death. The absence of oxygen leads to tissue acidosis as a result of anaerobic metabolism and lactate production. The mechanism by which hyperglycemia results in poorer outcomes following neurologic injury is postulated to be because it provides a further substrate for continued anaerobic metabolism.

The excitotoxicity drives the activation of neuronal and inducible nitric oxide synthase (nNOS and iNOS, respectively) with the resultant NO production generating free radicals. Free radical–mediated DNA damage and damage to cell membranes result. Damage to cell membranes can further

TABLE 26.1 Intracranial Herniation Syndromes and Their Associated Clinical Features

Herniation Type	Structures Compressed	Complications and Features
Cingulate/Subfalcine	Anterior cerebral artery	Contralateral paresis of the leg
Mesial frontal lobe (cingulate gyrus) herniates under the falx cerebri to the contralateral side	Frontal horn of lateral ventricle	Hydrocephalus
Lateral (Uncal) Tentorial	Ipsilateral cranial nerve III	Ipsilateral fixed, dilated pupil
Mesial temporal lobe (uncus) herniates across tentorial incisura compressing the rostral brainstem (midbrain)	Ipsilateral cerebral peduncle	Contralateral hemiparesis
	Reticular activating formation	Impaired consciousness level
	Ipsilateral posterior cerebral artery within ambient cistern	Blindness from occipital lobe infarction
Kernohan Notch Syndrome	Contralateral cranial nerve III	Contralateral fixed, dilated pupil
Variant of lateral (uncal) tentorial herniation whereby compression of contralateral structures against the contralateral tentorial incisura occurs	Contralateral cerebral peduncle	Ipsilateral hemiparesis
Central/Diencephalic	Midbrain vertical gaze center	Loss of vertical up-gaze with tonic down-gaze
Diencephalic structures and midbrain are compressed and displaced either from inferior or superiorly across the tentorial incisura	Pontine structures	Bilateral fixed and pinpoint pupils
	Cardiorespiratory centers	Abnormal respiratory pattern Cushing reflex (bradycardia and hypertension) Cardiac arrest
Tonsillar	Cardiorespiratory center in the medulla	Abnormal respiratory pattern Cushing reflex (bradycardia and hypertension) Cardiac arrest
Cerebellar tonsils pass through the foramen magnum and compress the medulla and cervicomedullary junction	Motor control center	Decorticate or decerebrate posturing

impact worsening ionic gradients by impairing protein channels involved in ionic transport. DNA damage and ischemia result in the activation of an inflammatory cascade via the up-regulation and nuclear transcription of pro-inflammatory cytokines (eg, adhesion molecules). Inflammatory cell recruitment and activation increase (eg, microglia), all of which continues the free radical–mediated injury.

The disruption of ionic transport mechanisms as a result of cell membrane injury precipitates uptake of fluid from extracellular spaces resulting in neuronal swelling even in the presence of an intact blood-brain barrier (cytotoxic edema). The subsequent breakdown of the blood-brain barrier then also leads to vasogenic edema, as unregulated transport of plasma proteins into cells occurs, increasing the osmotic drive for fluid influx. Cerebral edema increases ICP, worsens perfusion, and exacerbates ischemia.

The combination of excitotoxicity, tissue acidosis, free radical production, inflammatory activation, and cellular edema independently and in combination produce mitochondrial activation together with the release of cytochrome C from mitochondrial membranes (this also occurs due to mitochondrial membrane injury). The effect is activation of caspases and other proteolytic enzymes, which leads to apoptosis and cell death.

Many of the pathophysiologic processes described earlier that contribute to ischemia-related injury although damaging in the acute phase are also critical in the long term as the eventual healing and repair process begins with these mechanisms. The restoration of autoregulation including CO_2 reactivity and eventual healing with the formation of (usually nonfunctional) scar tissue may take from 4 to 6 weeks.

Global and Focal Ischemia

Global ischemia occurs with a global reduction in CBF (eg, hypoxic-ischemia injury secondary to cardiac arrest). Focal ischemia results when there is a focal reduction in blood flow in a major vessel: the infarct core is the region usually supplied by the smallest arterioles and end arteries that rapidly undergoes irreversible cell death; the surrounding penumbra is a zone where there is evidence of neuronal dysfunction and electrical silence, but it has not yet undergone depolarization, excitotoxicity, and irreversible cell death. This penumbra can be salvaged with restoration of CBF. Failure to restore perfusion will progressively incorporate the penumbra into the core infarct and increase its size. The vascular flow thresholds at which stepwise deterioration occurs vary depending on the basal metabolic activity of the region (eg, gray matter will intrinsically have higher metabolic rates and higher CBF

TABLE 26.2 Vascular Thresholds for Neuronal Ischemic Injury and Patterns of Dysfunction

Cerebral Blood Flow Threshold (mL/100 g of tissue/min)	Impact on Neuronal Function
30	Minimum vascular flow rate for maintaining neuronal function
20–30	Neuronal dysfunction with EEG slowing
10–20	Reversible neuronal dysfunction with salvage possible on restoration of cerebral blood flow EEG suppressed, evoked potentials absent Continued progressive impairment of perfusion will result in delayed neuronal death
<10	Irreversible neuronal dysfunction and cell death Total energy failure with loss of ionic balance, depolarization, and excitotoxicity

requirements in comparison to white matter), but on average CBF < 8 to 10 mL/100 g of tissue/min results in irreversible neuronal death (Table 26.2).

The size of the penumbra and core depends on the strength of the collateral supply to the region, and principles underpinning the use of perfusion imaging are intended to help characterize the relative proportions of the core infarct versus the penumbra, which helps to predict the impact of salvage and reperfusion therapy and to guide prognosis.

Initial Assessment of Critically Ill Neurosurgical Patients

A systematic approach is employed for assessing any critically ill neurosurgical patient. A variety of approaches exist, pioneered by trauma societies (Advanced Trauma Life Support [ATLS]),[7] resuscitation councils (Advanced Life Support [ALS]), and critical care and surgical societies (Care of the Critically Ill Surgical Patient [CCrISP]).[8] The basic principles are similar: a systematic, methodical, and reproducible approach to identify, resuscitate, and treat life-threatening insults in the most important sequence in which they occur—that is, airway (A), breathing (B) and respiratory function, circulatory (C) and cardiovascular function with fluid resuscitation, neurologic status and disability (D), and overall exposure (E) and assessment of other organ systems—the "ABCDE" approach. In trauma and neurosurgical patients, consideration is always given to the cervical spine, especially in patients at risk of spinal instability and spinal cord injury, and precautions are taken to preserve immobilization. Adherence to such a systematic method ensures that all practitioners have a

TABLE 26.3 Indications for Intubation and Ventilation in Critically Ill Neurosurgical Patients Presented in a Systematic "ABCDE" Manner

System Affected	Examples of Pathologic Processes
Airway	Airway injury with risk of obstruction (eg, major neck trauma in context of head injury, burns with high risk of airway edema, anaphylaxis)
Breathing and respiratory dysfunction	Lung injury (eg, major trauma with pulmonary injury) Respiratory failure (eg, neurogenic pulmonary edema, infection and aspiration pneumonia, pulmonary venous thromboembolism)
Circulation and cardiovascular dysfunction	Impaired cardiac function (eg, major trauma with cardiac injury)
Disability and neurologic dysfunction	Loss of airway reflexes (eg, decreased consciousness level, brainstem or cranial nerve injury with lack of gag reflex, high cervical spinal cord injury) Intracranial pressure control Status epilepticus
Exposure and other organ systems	Acid-base dysfunction Severe sepsis

methodical way to approach and assess any critically ill neurosurgical patient, identify physiologic derangement, and communicate with other medical personnel in a consistent manner while optimizing the patient's physiologic status. In neurosurgical patients, the goal is maintenance of cerebral (and spinal) oxygenation and perfusion, and control of intracranial pressure to limit secondary injury to the nervous system to achieve optimal outcomes.

Airway

Maintenance of a patent airway for adequate oxygenation is paramount: the brain is exquisitely sensitive to hypoxia and hypercapnia with significant effects on CBF, CPP, and ICP control. Deterioration in consciousness level also compromises the ability to protect the airway, increasing the risk of airway obstruction and aspiration. A variety of techniques exist for the purposes of airway control ranging from simple airway maneuvers (eg, "jaw thrust"), to the use of adjuncts (eg, oropharyngeal, nasopharyngeal, laryngeal mask airways), to definitive endotracheal intubation. Table 26.3 summarizes some indications to consider the use of intubation and mechanical ventilation in critically ill neurosurgical patients.

In the elective postoperative phase, causes of airway obstruction may relate to airway edema or hematoma (eg, following anterior cervical spine approaches, carotid endarterectomy) or, in posterior fossa surgery, dysfunction of the brainstem and lower cranial nerves.

Breathing and Respiratory Function

A rapid assessment of pulmonary function must be made to exclude any acute pulmonary causes for neurologic deterioration. In trauma patients in particular, acute life-threatening injuries such as tension pneumothorax, open pneumothorax, hemothorax, and flail chest must be excluded. In the early postoperative phase following elective surgery, pneumothorax may be a complication following central venous catheter insertion. In previously stable patients pulmonary infection, pulmonary edema (cardiac in origin or neurogenic secondary to a sympathetic surge following subarachnoid hemorrhage), and pulmonary venous thromboembolism are all important differentials to exclude with appropriately directed investigations in the setting of a pulmonary deterioration.

Circulatory, Cardiovascular Function, and Fluid Resuscitation

Ensuring stable hemodynamic function with adequate cerebral perfusion pressures is critical in neurosurgical patients. In patients with traumatic brain injury (TBI), severe hypotension (systolic blood pressure < 80 mm Hg) is a noteworthy independent factor contributing significantly to poor outcome and impacting mortality. Extrapolating this concept to ensure that hypovolemia and hypotension are identified and rapidly corrected in most neurosurgical pathologies is of paramount importance. In patients with cerebral vasospasm following subarachnoid hemorrhage, hypovolemia and hypotension can accelerate ischemic injury. In trauma patients, cardiac tamponade should be excluded.

Although a degree of hypertension may be tolerated—in patients with raised ICP, mass lesions, or subarachnoid hemorrhage, an intensive sympathetic activation may occur to drive cerebral perfusion pressures and maintain cerebral blood flow—significant hypertension (eg, systolic blood pressure > 180 mm Hg or mean arterial pressures > 120 mm Hg) itself may lead to adverse neurologic outcomes especially in the context of intracranial hemorrhage (eg, the presence of ruptured unsecured aneurysms) or in the early postoperative phase following cranial or spinal surgery, where operative hemostasis may be disrupted and precipitation of hemorrhage within surgical field may occur.

Causes for cardiac dysfunction may include primary cardiac pathologies (eg, myocardial infarction especially in patients with preexisting cardiovascular morbidities), hemorrhage in other organ systems in the setting of major trauma (eg, abdominal injuries, pelvic injuries), or may be related to sepsis or neurology (raised ICP, brainstem dysfunction, excessive sympathetic activation following subarachnoid hemorrhage, spinal cord injury with neurogenic shock, sympathetic disruption, and autonomic hyperreflexia following spinal injury). Fluid resuscitation together with cardiorespiratory support with invasive hemodynamic monitoring and inotropic support may be indicated.

Neurologic Status and Disability

Neurologic assessment in a critically ill neurosurgical patient must be rapid but systematic and focused. Airway protection, oxygenation, and optimization of hemodynamic status and cerebral perfusion should have already occurred as detailed earlier. Evaluation must include (1) an assessment of consciousness level; (2) pupillary size, light response, and reactivity; and (3) motor assessment of upper and lower extremities. More detailed and complete examination (eg, complete cranial nerve function, detailed cognitive assessment) should be performed if the hemodynamic and neurologic stability of the patient permits.

A variety of scores exist for evaluating consciousness level. The Glasgow Coma Score (GCS) is one example.[9] Strengths include the ease of application, good inter- and intraobserver reproducibility, and its ability to capture neurologic deterioration anatomically based on the sequential structures affected, and the fact that motor score in particular correlates with prognosis and outcome. Limitations such as the inability to evaluate the verbal component in intubated patients and lack of assessment and incorporation of brainstem reflexes have resulted in the development of other tools (eg, the FOUR Score).[10] Nonetheless the GCS remains one of the most widely used scores for urgent assessment of consciousness level and neurologic deterioration, as well as patient stratification in research (Table 26.4).

The causes of neurologic deterioration and impairment in consciousness level may be structural (with specific neurosurgical pathologies having stereotypical complications that need to be excluded; Table 26.5) or secondary to seizures or other metabolic and physiologic factors (eg, airway related, hypoxia, hypercapnia, hemodynamic abnormalities, temperature, electrolytes, blood glucose, acid-base dysfunction, and pharmacologic including hypnotic, sedative, and opioid excess).

Deterioration may manifest itself clinically with a progressive or sudden change in consciousness level or features of cerebral herniation (see Table 26.1). In intubated and ventilated patients, neurologic deterioration may manifest with the progressive changes in invasive monitoring parameters (ICP, $PbtO_2$, or hemodynamics). In awake patients, clinical features of raised intracranial pressure include headache, nausea, and vomiting; neurologic deficits including false localizing signs (eg, sixth cranial nerve palsy secondary to generalized increase in ICP); and papilledema (a late sign). The absence of papilledema does not exclude raised ICP. Its presence is merely indicative of chronically elevated intracranial pressure with transmission through the optic nerve sheath in communication with the subarachnoid space. Radiologic correlates of raised ICP on imaging that must be identified when assessing imaging in neurologically deteriorating patients are based on the neurophysiologic compensatory measures: displacement of intracranial CSF into lumbar cisterns manifests as loss of sulcal CSF spaces, obliteration of basal cisterns, collapsed and slit-like ventricles; cerebral herniation syndromes may be manifest on radiologic imaging such as uncal herniation across the tentorium, subfalcine and

TABLE 26.4 Examples of Two Mechanisms of Assessment of Consciousness Level in Neurosurgical Patients: the Glasgow Coma Score (GCS) and the FOUR Score

Component Assessed		GCS	FOUR
Eyes	4	Open spontaneously	Open, tracking, blinking to command
	3	Open to voice	Open, *not* tracking
	2	Open to pain	Open to loud voice
	1	Closed	Open to pain
	0	N/A	Closed
	Total Eye Score	**4** (min = 1; max = 4)	**4** (min = 0; max = 4)
Verbal	5	Alert and orientated to time, place, and person	Not incorporated
	4	Confused conversation	
	3	Inappropriate words	
	2	Inappropriate sounds	
	1	No verbalization	
	0	N/A	
	Total Verbal Score	**5** (min = 1; max = 5)	
Motor	6	Obeys commands	N/A
	5	Localizes to painful stimulus	
	4	Withdraws to painful stimulus	Thumbs up, fist, peace sign
	3	Abnormal flexion response (decorticate posture)	Localizes to painful stimulus
	2	Abnormal extension response (decerebrate posture)	Flexion response to pain
	1	No response	Extension response to pain
	0	N/A	No response or generalized myoclonic response
	Total Motor Score	**6** (min = 1; max = 6)	**4** (min = 0; max = 4)
Brainstem reflexes	4	Not incorporated	Pupil and corneal reflex present
	3		1 pupil fixed and dilated
	2		Pupil *or* corneal reflex absent
	1		Pupil *and* corneal reflex absent
	0		Absent pupil, corneal, and cough reflexes
	Total Score		**4** (min = 0; max = 4)
Respiration	4	Not incorporated	*Not* intubated, regular breathing
	3		*Not* intubated, Cheyne-Stokes respiration
	2		*Not* intubated, irregular breathing
	1		Intubated, triggering breaths on ventilator
	0		Intubated, *not* triggering breaths on ventilator
	Total Score		**4** (min = 0; max = 4)
TOTAL Score		Out of 15 *Max = 15* *Min = 3*	Out of 20 *Max = 20* *Min = 0*

N/A, not applicable.

TABLE 26.5 Causes of Neurologic Deterioration in Critically Ill Neurosurgical Patients

Neurosurgical Pathology	Possible Cause for Neurologic Deterioration
Traumatic brain injury	Generalized malignant cerebral edema Evolution of contusions Extension of hematoma Seizures Delayed hydrocephalus
Aneurysmal subarachnoid hemorrhage	Rebleeding Vasospasm and ischemia Hydrocephalus Seizures Electrolyte (predominantly sodium) dysfunction
Intracerebral hemorrhage	Extension of hematoma Hydrocephalus secondary to either intraventricular rupture *or* displacement-obstruction of ventricular system Seizures
Cerebellar hemorrhage	Brainstem compression Extension of hematoma Hydrocephalus (fourth ventricular obstruction)
Postoperative (eg, resection of tumor, spinal decompression)	Hemorrhage within surgical site *or* remote location Malignant cerebral edema Hydrocephalus Ischemic infarction Infection (superficial or deep surgical site)

tonsillar herniation, and brainstem compression at the foramen magnum.

The aim is to confirm that deterioration has occurred, to identify possible causes including the use of diagnostic imaging where required (eg, CT, MRI), and to anticipate the need for either surgical intervention or admission to, and management in, a neurocritical care setting if indicated.

Exposure and Other Organ System Assessment

Exposure entails a rapid assessment of the other major organ systems and correction of any other parameters that may be relevant in critically ill neurosurgical patients that may affect the outcome and possible neurosurgical intervention. For example, in patients with spinal cord injury, decompression of the gastric contents and bladder is imperative to avoid possible complications secondary to autonomic hyperreflexia. Other common considerations include an assessment of electrolytes, glucose and renal function, hematologic parameters that may increase risk of hemorrhage (eg, thrombocytopenia, pharmacologic anticoagulants), and excessive use of pharmacologic agents (eg, opioid overdose).

Basic Concepts of Management in Neurocritical Care Units

A variety of neurosurgical patients may require admission to an NCCU. These include (1) patients in the immediate postoperative phase following either elective or emergency surgery, (2) previously stable patients with a neurologic or systemic deterioration that require intensive care–level monitoring and management, and (3) critically ill neurosurgical patients admitted directly due to the severity of their condition. As with the assessment of a critically ill neurosurgical patient, a systematic approach is required when evaluating and managing patients in the NCCU to ensure that physiologic parameters are optimized and that there is close monitoring to detect any neurologic deterioration and achieve optimal outcomes. The mnemonic "ABCDE FLAT HUGS" is an aide-memoire of the critical parameters that require regular assessment (Table 26.6).

Airway and Ventilation

Hypoxia is a significant independent risk factor for worse outcomes and increasing mortality in the context of patients with traumatic brain injury. Critically ill neurosurgical patients should have a definitive assessment of airway patency, and steps should be taken to ensure it is secured as soon as possible.

Governance of Oxygen Delivery and Physiologic Concepts

Total O_2 content within the blood is based on (1) the amount of O_2 dissolved in plasma (as per Henry's law, dependent on the solubility of O_2 and PaO_2) and (2) the O_2–carrying capacity of hemoglobin (dependent on SaO_2 and the concentration of hemoglobin). Assuming a temperature of 37°C and a hemoglobin concentration ([Hb]) of 150 g/L, in arterial blood (with SaO_2 97% and PaO_2 13.3 kPa), there are approximately 200 mL of O_2/L; in mixed venous blood (SaO_2 75% and PaO_2 5.6 kPa) there are 150 mL of O_2/L. The degree of oxygen flux and usage is approximately 50 mL/L. With a cardiac output of 5 L/min, the oxygen flux and usage are 250 mL/min. Hence it is imperative to understand that oxygen delivery depends on temperature (which determines the solubility of O_2), cardiac output, PaO_2 and SaO_2, and hemoglobin concentration. The meticulous optimization of these parameters is vital to ensure adequate cerebral oxygenation and perfusion and therefore limit secondary injury.

The aim should be to provide adequate oxygenation and avoid hyper- or hypocapnia. Targets vary depending on the patient comorbid status, the presence of preexisting respiratory comorbidities, and clinical status, but where feasible, the aims should be oxygen saturation (SaO_2) ≥ 97%, PaO_2 ≥ 11 to 13 kPa, and $PaCO_2$ 4.7 to 5.3 kPa (normocapnia). Mechanisms to increase oxygenation include increasing the inspired oxygen fraction (FiO_2), increasing the inspiratory time to expiratory time cycling (IT:ET ratio from 1:2 to 2:2, respectively), and applying positive end-expiratory pressure (PEEP ≤ 10 mm Hg). Peak inspiratory pressures should not exceed

TABLE 26.6 Main Parameters That Require Regular Assessment and Monitoring in Neurocritical Care Units

System	Parameters
A—**A**irway	Adequacy of airway, type of airway (eg, endotracheal tube, tracheostomy)
B—**B**reathing	Respiratory rate, oxygen saturation (SaO_2), PaO_2, $PaCO_2$, acid-base status (pH, lactate, bicarbonate)
C—**C**irculation and **c**ardiovascular	Heart rate, rhythm, blood pressure
D—Neurologic **d**isability	Consciousness level (Glasgow Coma Score/FOUR Score), pupil size, symmetry and reactivity, peripheral limb motor and sensory function
E—**E**xposure and other organ systems	Temperature, renal function, electrolytes, fluid balance and urine output
F—**F**eeding	Enteral feeding if possible (or parenteral nutrition)
L—**L**ines and invasive monitoring	Invasive monitoring (if indicated): central venous pressure catheter, arterial line for invasive blood pressure, pulmonary artery catheter, urinary catheter
A—**A**nalgesia, **a**ntiepileptics, **a**ntimicrobials	Analgesia—verbal or visual scales for assessment, World Health Organization (WHO) analgesic ladder Antiepileptics—appropriate seizure control Antimicrobials—monitoring and treatment of infection
T—Venous **t**hromboembolism prophylaxis	Mechanical prophylaxis—thromboelastic stockings, pneumatic compression devices Pharmacologic prophylaxis (if indicated)—low-molecular-weight heparin, unfractionated heparin
H—**H**ead up and ICP stabilization measures	Elevate the head above heart and protocol driven strategy for ICP control
U—**U**lcer (gastric) prophylaxis and nausea/vomiting	Gastric protection against stress ulceration (eg, proton-pump inhibitors) and antiemetics
G—**G**lycemic control	Maintain glucose within normal range (4.4–8.3 mmol/L; 80–150 mg/dl)
S—**S**pecific neurologic monitoring and neurosurgical pathology-related concerns	Neurologic monitoring—ICP, $SjvO_2$, $PbtO_2$, TCD Special concerns depending on neurosurgical pathology (eg, postoperative steroids and electrolytes, osmolality and fluid balance following pituitary surgery)

"ABCDE FLAT HUGS" is an aide-memoire.
ICP, intracranial pressure; *$PaCO_2$,* arterial carbon dioxide tension; *PaO_2,* arterial oxygen tension; *$PbtO_2$,* brain tissue oxygen tension; *SaO_2,* oxygen saturation; *$SjvO_2$,* jugular venous oxygen saturation; *TCD,* transcranial Doppler.

35 mm Hg to ensure minimal interference with cerebral venous drainage.

Prophylactic hypocapnia via hyperventilation (minute ventilation [MV] = tidal volume [V_T] × ventilatory rate [V_R]) should be avoided, as it causes cerebral vascular vasoconstriction with the risk of worsening cerebral ischemia. For the purposes of ICP control, it is a short-term measure only until more definitive measures to control ICP are instituted. Patients that are intubated and on mechanical ventilation should have adequate sedation (intravenous hypnotic; eg, propofol, midazolam), analgesia (eg, opioid), and, if needed, a neuromuscular blocking agent to avoid ventilator-associated stress, gag, and the patient fighting against the ventilator—all of which can precipitate systemic hypertension, distress, and, via the transmission of increased intrathoracic pressures, an increase in ICP.

Attempts to wean the patient off the ventilator as soon as clinically feasible and aim for extubation should be considered. There are multiple benefits to this strategy, including the ability to perform a clinical neurologic examination and reduce the risk of ventilator-associated complications including ventilator-associated pneumonia (VAP). There are significant differences in the majority of critically ill neurosurgical patients in comparison to patients in general critical care units[1]: most will have normal baseline pulmonary function tests (except elderly patients with preexisting chronic obstructive pulmonary disease); most will require only synchronized intermittent mandatory ventilation (SIMV) or pressure support ventilation (PSV); and other strategies such as prone ventilation, permissive hypercapnia, and inverse ratio ventilation are usually avoided and rare. As such, ventilator dependence is less common with rapid weaning expected.

Exceptions may be patients with significant polytrauma or high cervical spinal cord injury. In situations where a prolonged period of mechanical ventilation is anticipated, consideration should be made for early tracheostomy (performed as an open surgical procedure or percutaneous). Benefits include increasing patient comfort and ability to tolerate tracheal tubes without significant gag, thereby allowing neurologic examination without sedation to occur more easily, improved length of NCCU stay, more effective airway clearance and bronchial

toilet of secretions, and a decreased risk of tracheolaryngeal stenosis secondary to prolonged intubation.

Circulation and Cardiovascular Function

Apart from some specific circumstances (eg, aSAH-associated vasospasm where hypervolemia may be indicated), in most critically ill neurosurgical patients, the aim is to arrive at normovolemia and normotension to achieve stable cerebral perfusion. Basic equations pertaining to cardiovascular function include the following:

1. Cardiac output (CO) = Stroke volume (SV) × Heart rate (HR)
2. Blood pressure (BP) = Systemic vascular resistance (SVR) × Cardiac output (CO)
3. Pulse pressure (PP) = Systolic blood pressure (SBP) – Diastolic blood pressure (DBP)
4. Mean arterial pressure (MAP) = (⅔ DBP + ⅓ SBP) or (DBP + ⅓ PP)

Circulatory and fluid status and cardiovascular function may be monitored using noninvasive or invasive means, and this involves a combination of clinical and biochemical parameters. Clinical parameters include body weight, HR, BP, and hourly assessment of input-output fluid balance including urinary output. Biochemical parameters include hematocrit, acid-base status including lactate, electrolytes (sodium), renal function (urea and creatinine), serum and urine osmolalities, and urine specific gravity. Invasive hemodynamic monitoring techniques[11] include the use of central venous pressure (CVP) or, in certain circumstances, pulmonary artery flotation catheters (PAFCs). The former is especially useful to guide the adequacy of fluid resuscitation especially in circumstances where osmotic diuresis (eg, mannitol, furosemide) is used in ICP control, which makes use of urine output less reliable. The latter allows for the calculation of a variety of hemodynamic parameters including SVR, CO, and pulmonary artery capillary wedge pressure (PACWP)—all of which become important especially in the context of guiding fluid therapy and inotrope use. Trends of CVP and PACWP rather than absolute values are more indicative of fluid status. Some critical care specialists recommend the use of pulse pressure variability (% PPV) or systolic blood pressure variability (% SBPV) as a better predictor of response to fluid therapy.

Fluid and Electrolyte Management

In most neurosurgical pathologies, the aim of fluid resuscitation and management should be to achieve normovolemia, normal electrolytes, normal serum osmolalities, and normoglycemia. Daily fluid requirements are approximately 40 mL/kg/24 hr with hourly requirements calculated as (1) 4 mL/kg for every kilogram from 0 to 10 kg of body weight, (2) 2 mL/kg for every kilogram from 11 to 20 kg of body weight, and (3) 1 mL/kg for every kilogram of body weight from 20 kg onward. A urine output of 1 mL/kg/hour should be the aim to avoid oliguria. Fluid management should also take into consideration variable factors such as the impact of temperature, fever, and respiratory dysfunction on increasing insensible fluid losses; the impact of anesthesia and sedation-induced cardiac depression and vasodilation; preoperative or perioperative deficits; and the redistribution of third space fluid losses. The daily sodium requirement is 1 to 2 mmol/kg (or mEq/kg), and the daily potassium requirement is 0.5 to 1 mmol/kg (or mEq/kg).

Fluid Compartments in the Body and Types of Intravenous Fluid Therapy

Fluid compartments in the body consist of the intracellular fluid (ICF) to extracellular fluid (ECF) compartments with the distribution ratio being 2:3 to 1:3, respectively. The ECF compartment is further divided into intravascular (I_{Vasc}) and extravascular (E_{Vasc}) spaces. The ratio of the I_{Vasc} (circulating volume) to E_{Vasc} (interstitial space, lymph, transcellular spaces) is 1:4 to 3:4.

Routine IV fluid therapy in neurosurgical patients should be restricted to the use of 0.9% saline or physiologically balanced salt solutions (eg, lactated Ringer's, Hartmann's). These crystalloid solutions are isotonic (iso-osmolar) with respect to human plasma and therefore only distribute within the ECF compartment appropriately (ie, one-fourth of the infused volume remains in the I_{Vasc} and three-fourths distribute within the E_{Vasc} space. Hypotonic (or hypo-osmolar) solutions such as 5% dextrose (essentially dextrose in water) should be strictly avoided in neurosurgical patients. On infusion, the dextrose is metabolized leaving hypotonic water, which distributes rapidly in both the ICF and ECF compartments. There are three possible complications: (1) only one-twelfth (one-third in the ECF of which only one-fourth is I_{Vasc}; ie, ⅓ × ¼) of the original infused volume remains in the I_{Vasc} space, and therefore its use as a fluid resuscitation agent is limited, (2) the distribution into the ICF compartment can precipitate an increase in cellular and cerebral edema and cause ICP elevation, and (3) the hyperglycemia state associated with dextrose may be associated with poorer outcomes in critically ill neurosurgical patients.

Hyperosmolar and Osmotic Diuretic Therapy

Examples of hyperosmolar and osmotic diuretic therapy include mannitol and hypertonic saline (in a variety of strength solutions including 1.8%, 3%, 5%, and 23.4%). There are two specific uses in neurosurgical patients. The first and most common is in the management of raised ICP and cerebral edema. Mannitol (0.5–1 g/kg bolus dosing) is hypothesized to work through a variety of mechanisms: (1) creation of an osmotic gradient within the intravascular space (in the presence of an intact blood-brain barrier) drawing fluid from the cerebral intracellular compartment; (2) improvement in blood rheology secondary to a dehydration within the red cells and alteration of the red cell morphology allowing easier passage through cerebral vessels transiently, which increases cerebral blood flow and precipitates an autoregulation-mediated vasoconstriction and associated blood flow reduction; and (3) action as a free radical scavenger to limit inflammatory mediated injury and apoptosis. The main complications include generation of an osmotic diuresis with intravascular volume depletion, which in itself may precipitate hypotension in

patients with preexisting volume depletion and potentiate secondary injury. Furthermore, in the presence of a damaged blood-brain barrier, mannitol can theoretically cross into the intracellular compartment or interstitial spaces, increasing cerebral edema and subsequently ICP. It should not be used prophylactically therefore and only as a short-term salvage therapy to treat life-threatening intracranial hypertension. It is imperative that patients using mannitol have a urinary catheter in place for accurate urine output measurement and to ensure that serum osmolality (≤320 mOsm/L should be maintained) and sodium (Na^+ < 155 mmol/L should be maintained) are monitored. If ICP no longer responds significantly to mannitol, its use should be discontinued.

Hypertonic saline is another effective hyperosmolar agent to reduce and control intracranial hypertension.[12] It has the added effect of being an effective intravascular volume expansion agent—leading to its secondary use in fluid resuscitation in trauma settings to improve circulating volume—without the associated osmotic diuresis associated with mannitol, and therefore MAP/CPP is more stable during its use. In addition it may have a longer duration of action compared to mannitol. Serum sodium concentration must be monitored, and use should be discontinued if serum sodium is > 155 mmol/L. Difficulties using hypertonic saline include the risk of nonanion gap metabolic acidosis, an unknown optimal dosing strategy and the irritant effect on peripheral veins when infused through peripheral rather than central venous catheters. Table 26.7 highlights the approximate sodium concentrations within the commonly used hypertonic saline solutions.

Blood Pressure Control

Stringent control of blood pressure is a vital component of the critical care management of neurosurgical patients. Blood pressure targets should always be individualized taking into consideration the setting (eg, postoperative from elective surgery, postoperative following emergency surgery, vasospasm following aSAH, management of severe TBI) and the patient's preexisting blood pressure (eg, normotensive or hypertensive).

Causes of increased blood pressure may include physiologic stress (eg, pain, anxiety, agitation), ventilator-associated stress due to inadequate sedation/muscle relaxation, the cerebral autoregulation response in order to improve perfusion in cerebral ischemia, the presence of preexisting hypertension (the autoregulation curve is shifted to the right with a higher plateau and range for autoregulation), and the Cushing reflex (hypertension, bradycardia, and altered respiratory patterns that either may be indicative of medullary ischemia secondary to impending tonsillar herniation or may be a compensatory response to a global reduction in CPP secondary to raised ICP to preserve cerebral perfusion).

Complications of uncontrolled hypertension include increasing cerebral edema, expansion of intracranial hemorrhagic lesions, and cardiopulmonary dysfunction including pulmonary edema and renal dysfunction. Neurosurgical pathology-related complications include re-rupture of unsecured aneurysms following aSAH and disruption of intraoperative hemostasis within the surgical field following surgery and precipitation of postoperative hemorrhage. A compromise therefore must be made to ensure sufficient blood pressure to maintain cerebral perfusion while avoiding extremes that risk hemorrhage.

In most circumstances, SBP > 180 mm Hg or MAP > 120 mm Hg should be avoided.[1] Pharmacologic agents used to treat hypertension include labetalol boluses (eg, 20–40 mg) and hydralazine 20 mg (in the presence of significant bradycardia). Labetalol or nicardipine infusions (starting with an initial dose of 5 mg/hour and titrating under close invasive monitoring) may be required for persistent hypertension.

TABLE 26.7 Sodium Concentrations Within the Commonly Used Hypertonic Saline Solutions

Sodium Chloride (NaCl) Concentration	Sodium Concentration (mmol or mEq in 1 L of Fluid)
0.9%	154
1.8%	308
3%	513
5%	856
23.4%	4004

Neurologic Assessment and Disability

Regular neurologic assessment to identify early on any neurologic deterioration is crucial with appropriate investigation and management (discussed earlier).

Exposure and Other Organ Systems

Adequate monitoring of urine output, fluid balance status, and electrolytes is crucial. A variety of derangements in electrolytes may occur in sodium, potassium, magnesium, calcium, and phosphate. These must be identified early and corrected (discussed later).

Feeding and Nutrition

Establishing early enteral feeding and nutrition is an important part of the management of critically ill neurosurgical patients.[13] The body undergoes a highly stereotypical metabolic response to any form of injury (including iatrogenically as a response to the trauma of surgery) or major trauma regulated by a variety of systemic hormonal systems including antidiuretic hormone (ADH), aldosterone, catecholamines, cortisol and adrenocorticotropic hormone (ACTH), growth hormone (GH), and glucagon. The metabolic response is classically divided into phases depending on the metabolic rate: the ebb or shock phase (24–48 hours with a decrease in basal metabolic rate [BMR]), the flow phase with severe catabolism (3–10 days with increase in BMR), and finally a recovery phase with anabolism (may last weeks to months with a decrease in BMR back to normal). The physiologic result, especially in the

catabolic phase, is increased energy expenditure, increased protein catabolism, and a state of impaired glucose tolerance with hyperglycemia with associated complications such as immune suppression, organ and enzyme dysfunction, wound healing impairment, muscle wasting, and weakness (which may impair respiratory muscle function affecting respiratory drive, lung defense mechanisms, and success of ventilatory weaning). It is therefore imperative that nutritional needs are adjusted and calculated to account for this metabolic response and immediately initiated to optimize the chance of recovery and outcome. Early input from dietitian specialists is recommended.

Enteral nutrition is by far the preferred method for nutritional supplementation; it maintains the integrity of the gastrointestinal tract and mucosal barrier preventing translocation of microbes into the systemic circulation, which is postulated to be a key etiologic factor in the development of the systemic inflammatory response syndrome (SIRS) and multiorgan dysfunction syndrome (MODS) in critically ill patients. Modes of enteral nutrition include nasogastric and nasojejunal feeding in the short term, but if there is anticipation that swallowing mechanisms will be impaired in the long term, gastrostomy or jejunostomy placement may be required. Parenteral nutrition is associated with more metabolic and access-related complications compared to enteral nutrition and is only indicated in the presence of severe gastrointestinal injury where enteral feeding is not possible (eg, major polytrauma); it requires more intensive monitoring of serum electrolytes and other parameters (eg, glucose, phosphate, magnesium).

Principles of Neurologic Monitoring

Neurologic monitoring is a key aspect of patient care and management in critically ill neurosurgical patients.[14,15] A variety of invasive (eg, ICP monitoring, jugular venous oximetry, brain tissue oxygenation, cerebral microdialysis) and noninvasive (eg, transcranial Doppler ultrasonography, electroencephalography) techniques may be implemented.

Intracranial Pressure Monitoring

Arguably the most common and widely used modality, ICP monitoring is used to guide management of critically ill neurosurgical patients in whom clinical assessment is not possible due to either significantly impaired consciousness level or intubation and sedation. It allows calculation of CPP (MAP – ICP) as well as other parameters such as the cerebrovascular pressure reactivity index (PRx), which reflects the autoregulatory reserve and compliance of the cerebrovasculature. The trend and variability in ICP over a time period, analysis of its waveform, and correlation with other clinical variables are far more informative in making clinical management decisions than a single, isolated ICP valve. Most of the evidence-based parameters regarding ICP (and by extension CPP) treatment thresholds are based on outcomes in cohorts of patients with traumatic brain injury (TBI)[16]; in severe TBI, average ICP > 25 mm Hg is associated with a twofold increase in risk of death. In general, ICP > 20 to 25 mm Hg is considered abnormal, and if persistent it is an indication for initiating aggressive treatment measures. Table 26.8 summarizes the advantages and disadvantages of currently available ICP monitoring techniques. Brain Trauma Foundation (BTF) guidance recommends ICP monitoring in the following situations:

- Patients with GCS ≤ 8 post resuscitation and an abnormal CT head scan
- Patients with GCS ≤ 8 post resuscitation with a normal CT Head scan with two out of the three following risk factors:
  - Age ≥ 40 years,
  - SBP < 90 mm Hg
  - Unilateral or bilateral motor posturing

TABLE 26.8 Invasive Techniques for Monitoring Intracranial Pressure

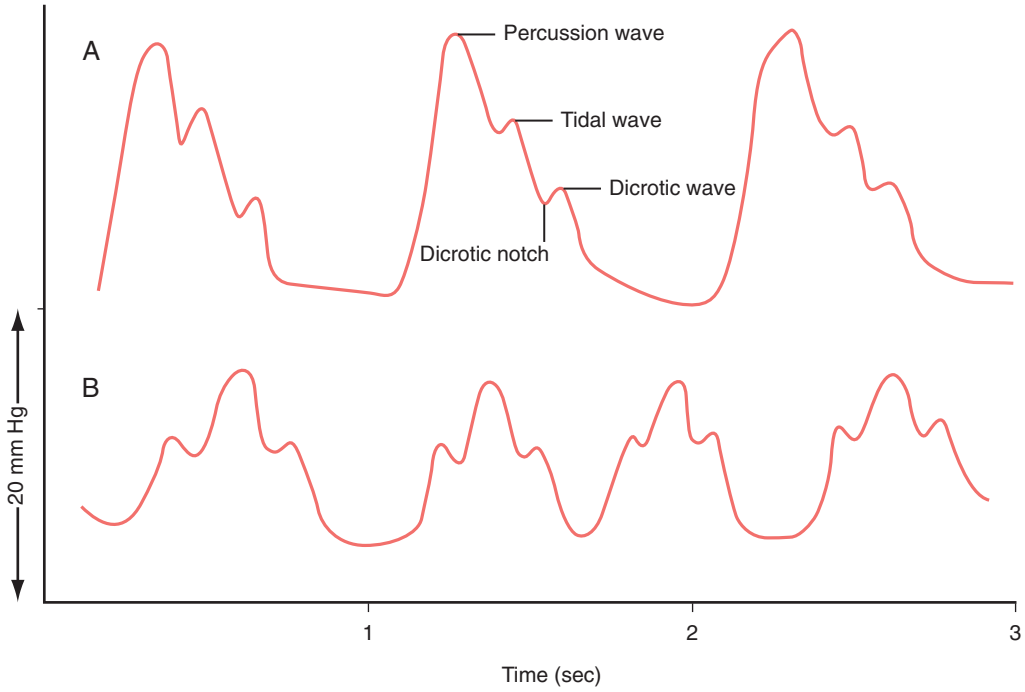
Technique		Advantages	Disadvantages
Intraventricular catheter connected to external pressure transducer		Gold standard Diagnostic and therapeutic allowing CSF drainage Can be recalibrated and rezeroed noninvasively	Infection risk Hemorrhage risk Difficult in patients with severe brain swelling with obliterated ventricular system
Fiberoptic micro transducer tipped catheter system	Intraparenchymal	Reduced infection risk Can be inserted in edematous brain	Risk of "drift" Cannot be recalibrated or rezeroed Reflects only "local" ICP near transducer and may not reflect ICP and ventricular cerebrospinal fluid pressure in other compartments
	Subdural or epidural	Least invasive	Reliability and accuracy Precise relationship between extraaxial pressure and ICP not yet established

ICP, intracranial pressure.

- Patients with GCS > 8 in whom assessment of neurologic status to monitor for neurologic deterioration is unreliable or not possible (eg, sedation, intubation, and paralysis)

The ICP waveform has three characteristic peaks[4]: (1) P1 (percussion: reflecting the arterial systolic pressure wave at peak cardiac systole transmitted throughout the choroid plexus); (2) P2 (tidal: a rebound increase in ICP that occurs with the increase in intracranial volume from the intracranial arteries filling with systolic blood; it is a strong indicator of brain compliance with P2 normally ~ 80% of P1; in pathologic states of impaired intracranial compliance, P2 peak is greater than P1; Fig. 26.6); and P3 (dicrotic: reflects transmission of aortic valve closure). A variety of common ICP waveform patterns may be observed (Table 26.9).[17]

The cerebrovascular pressure reactivity index (PRx) is another variable that may be extrapolated from ICP monitoring. Although not in routine use, there is increasing evidence that together with analysis of the ICP pulse waveform, it provides useful information regarding the autoregulatory reserve of cerebral vasculature and the adequacy of CPP. In patients



• **Figure 26.6** Intracranial pressure (ICP) waveform. (A) The normal ICP waveform seen under physiologic conditions with three peaks: percussion, tidal, and dicrotic. (B) An abnormal ICP waveform in a situation with raised ICP and reduced intracranial compliance. The P2 (tidal) wave peak is greater than the P1 (percussion) wave peak. The lack of intracranial compliance means that the increase in ICP from increased intracranial volume due to intracranial vessels filling with arterial systolic blood is greater than the amplitude of the original percussion P1 wave.

TABLE 26.9 Common Intracranial Pressure Patterns and Pathologic Waveforms

Pattern	Description	Significance
Low and stable	ICP < 20 mm Hg	Uncomplicated head injury Early trauma phase
High and stable	ICP > 20 mm Hg	Most common pattern after head injury
Lundberg A—Plateau	Abrupt elevation of ICP Lasts 5 to 20 minutes Mean wave amplitude may be > 50 mm Hg Return to elevated baseline	Reflects decreased brain compliance with ↑ ICP, ↓ CPP and ischemia Heralds prodrome of neurologic deterioration Urgent intervention recommended
Lundberg B—Vasogenic	Mean waves of lower peak pressure (20–50 mm Hg) lasting for a shorter time (30 s–3 min)	May be physiologic Related to respiratory fluctuations (frequency mirrors respiratory cycle: 8–20/min)

CPP, cerebral perfusion pressure; *ICP,* intracranial pressure.

with intact cerebral autoregulation, ↑ MAP leads to reflex vasoconstriction with ↓ in CBV and ICP. When autoregulation is dysfunctional, vessel vasodilation occurs with ↑ MAP, leading to ↑ CBV and ICP. PRx is a correlation coefficient between slow changes in arterial blood pressure and ICP. A negative PRx (<0.3) suggests preserved cerebrovascular autoregulatory capacity, whereas a positive PRx (> 0.3) reflects dysfunctional cerebrovascular autoregulation (ICP follows MAP in linear fashion) and may be associated with poorer outcomes. The PRx may also be used to calculate optimal CPP targets for individuals by plotting PRx (y-axis) against CPP (x-axis) and evaluating the resulting curve (usually "U" shaped with the base reflecting optimal CPP range with the lowest valve for PRx).

Cerebral Oxygenation

Monitoring cerebral oxygenation is becoming routine in NCCUs, as ICP monitoring alone cannot detect the cerebral ischemia and hypoxia that accompanies and exacerbates primary and secondary brain injury.[18,19] Two principal methods exist: (1) jugular venous oximetry with $SjvO_2$ and (2) brain tissue oxygen tension ($PbtO_2$).

Jugular Venous Oximetry

Placement of a catheter with a fiberoptic transducer in the jugular bulb allows sampling of venous blood directly from the intracranial circulation with the jugular venous oxygen saturation ($SjvO_2$) allowing estimation of global cerebral oxygenation, metabolism, oxygen extraction by the brain, and calculation of the arteriovenous oxygen gradient (A-V DO_2). $SjvO_2$ reflects the balance between cerebral oxygen delivery (~CBF) and cerebral metabolic demand/oxygen consumption (~CMR O_2) (Table 26.10).

As with ICP monitoring, $SjvO_2$ should be evaluated in conjunction with parameters (eg, MAP, PaO_2, $PaCO_2$, $PbtO_2$; discussed later) to guide therapeutic interventions. For example, the therapeutic efficacy of hyperventilation may also be monitored with $SjvO_2$, as prolonged vasoconstriction associated with hypocapnia may lead to ischemia and this may be reflected in abnormally ↓ $SjvO_2$ necessitating termination of hyperventilation therapy.

Limitations of jugular venous oximetry include (1) reflection of global cerebral oxygenation rather than specific regional variations, (2) thrombotic complications affecting jugular veins, (3) malposition of catheters and variability from changes in head position, and (4) errors due to the inclusion of extracranial blood (eg, from a common facial vein).

Brain Tissue Oxygen Tension

Probes inserted directly into the brain parenchyma can measure brain tissue oxygen tension ($PbtO_2$ – partial pressure of oxygen in brain tissue), which acts as an adjunct and surrogate of cerebral oxygenation. Similar to $SjvO_2$, it reflects a balance between cerebral oxygen delivery and cerebral metabolic demand/oxygen consumption. Modern probes allow simultaneous measurement of ICP and brain tissue temperature. The aim is for early detection of cerebral ischemia and hypoxia (even in the presence of normal MAP, CPP, and ICP). Normal values range between 25 and 30 mm Hg with values < 10 mm Hg considered pathologic and reflective of severe ischemia.

TABLE 26.10 Normal Thresholds for $SjvO_2$ and Causes of Deviation

$SjvO_2$ Value	Significance	Etiology
55%–75%	Normal	Nil
<55%	↓ O_2 delivery with ischemia	↓ CBF (due to ↑ ICP, ↓ MAP, vasospasm, hyperventilation associated with ↓ $PaCO_2$ with resultant vasoconstriction) Global hypoxia (↓ PaO_2, ↓ [Hb])
	↑ O_2 consumption and cerebral metabolic demand	Fever, seizures, pain, agitation and stress with inadequate sedation
>75%	↑ O_2 delivery with luxury perfusion and hyperemia	Pathologic ↑ in CBF (eg, dysfunctional autoregulation, traumatic arteriovenous fistula) Overtreatment of cardiorespiratory insufficiency with global hyperoxia (↑ PaO_2)
	↓ O_2 consumption and cerebral metabolic demand	Deep sedation (eg, barbiturates), hypothermia, cerebral infarction and brain death

CBF, cerebral blood flow; *ICP,* intracranial pressure; *MAP,* mean arterial pressure.

The interpretation of $PbtO_2$ is almost identical to that of $SjvO_2$: ↓ $PbtO_2$ and ↓ $SjvO_2$ reflect either (1) impaired O_2 delivery, with ischemia (due to either ↓ CBF or global hypoxemia) or (2) excessive O_2 consumption and metabolic demand, and vice versa (see Table 26.10). As with other forms of invasive neuromonitoring, $PbtO_2$ should be interpreted in conjunction with other parameters such as ICP and $SjvO_2$:

- ↓ $SjvO_2$ and ↓ $PbtO_2$ with ↑ ICP suggests that cerebral oxygenation and CPP are impaired secondary to raised ICP and intervention aimed at identifying and treating the cause for the raised ICP.
- ↓ $SjvO_2$ and ↓ $PbtO_2$ with normal or ↓ ICP suggests that the impairment in cerebral oxygenation and CPP may reflect non-ICP related causes (eg, global hypotension, vasoconstriction secondary to hypocapnia, global hypoxemia).
- ↑ $SjvO_2$ and ↑ $PbtO_2$ with ↑ ICP may suggest impairment in cerebral autoregulation with abnormally increased CBF with hyperemia, and the treatment may require

hyperventilation to promote hypocapnia and reduce CBV and CBF.
- ↑ $SjvO_2$ and ↑ $PbtO_2$ with ↓ ICP may suggest reduced demand due to deep (eg, barbiturate induced) sedation or hypothermia.

Limitations are that only the oxygenation of tissue local to the site of the probe is assessed as opposed to $SjvO_2$, which provides a global measure of cerebral oxygenation. However, this could be considered an advantage in certain circumstances where one could selectively monitor at-risk tissue. It is invasive and associated with complications such as hemorrhage, which can affect the accuracy of the recordings. Controversy also exists as to the optimal location of probes: radiologically normal brain (to fulfill its utility to detect early on cerebral hypoxia and ischemia in areas with normal ICP, MAP, and CPP) or perilesional tissue (eg, ischemic penumbra or at-risk tissue near injured brain).

Transcranial Doppler Ultrasonography

TCD is a noninvasive, real-time indirect measure of CBF. It allows the calculation of arterial blood flow velocity (FV), which closely correlates with changes in CBF. A variety of vessels may be "insonated" using the Doppler probe through the cranial bones:
- Transtemporal bone window—anterior cerebral (ACA), middle cerebral (MCA), posterior cerebral (PCA) arteries
- Suboccipital bone window—vertebral arteries (VA)
- Transorbital bone window—internal carotid artery (ICA) at the site of the carotid siphon
- Neck—extracranial ICA and the external carotid artery (ECA)

Limitations are that it is operator dependent with the angle of insonation (between vessel axis and the ultrasound beam) affecting velocity. The easiest vessel to assess reliably and the most common is the MCA, given the ease of access in terms of the thin bone of the pterion and the axis of direction of the vessel.

TCD is applied in a variety of settings including the following:
1. Detection of cerebral vasospasm following aneurysmal subarachnoid hemorrhage
   a. FV_{MCA} > 120 cm/second
   b. Lindegaard ratio (FV_{MCA}/FV_{ICA}) > 3
2. Assessment of cerebrovascular reactivity, autoregulatory reserve, and "threshold" ("break point")—CPP at which autoregulation fails—thereby estimating and providing CPP targets for optimizing treatment

Cerebral Microdialysis

Microdialysis utilizes catheter implantation directly into brain tissue to measure in vivo the concentration of biochemical substances and metabolites in the extracellular fluid. A variety of substances are measured including lactate, pyruvate, glucose (the lactate/pyruvate ratio being a marker of dysfunction in aerobic metabolism and therefore allowing early detection of ischemia), glutamate, and glycerol. Applications may not only be in the setting of traumatic brain injury, subarachnoid hemorrhage, and stroke, but also in intracranial tumors to possibly develop markers of tissue infiltration. Limitations are that it is operator dependent requiring highly trained personnel, invasive, and requires careful interpretation of results in relation to catheter location.

Electroencephalography

A useful adjunct in critically ill neurosurgical patients, electroencephalography (EEG) and other associated monitors of cerebral function (Bi Spectral Index [BIS] monitor, entropy) are helpful in assessing the depth of anesthesia and the depth of sedation and in evaluating patients for the presence of seizure activity (eg, nonconvulsive status epilepticus).

Multimodal Monitoring

Progressive advances in technology, innovation, and knowledge have increased the variety of techniques available for monitoring the primary facet in the management of critically ill neurosurgical patients—the prevention of cerebral ischemia and the optimization of cerebral oxygenation and cerebral perfusion. As with all monitoring techniques, trends and variability over the course of time provide a more useful assessment than isolated measurements, and the data obtained from each method of monitoring should be interpreted in conjunction with other parameters and a clinical assessment of the patient rather than in isolation to provide a true multimodal assessment and individualization of patient treatment.[20]

Specifics of General Care in Critically Ill Neurosurgical Patients

Common complications in managing critically ill neurosurgical patients include raised ICP, seizures and status epilepticus, infection, and electrolyte disorders. An understanding of concepts pertaining to pathophysiology and management is important.

Management of Raised Intracranial Pressure

Most units managing critically ill neurosurgical patients have introduced standardized management paradigms reflecting targets for ICP and CPP that have evolved from the importance of ICP control in the setting of TBI.[21] Despite the heterogeneous nature of neurosurgical pathophysiology in different etiologies, the overarching principle of maintenance of cerebral perfusion and oxygenation and prevention of ischemia is intimately linked to CPP and ICP. Therefore these principles may be applied in general to any critically ill neurosurgical patient.

The various mechanisms for ICP control and CPP are implemented in a stepwise escalation of therapeutic

TABLE 26.11 Management Strategies for Intracranial Pressure Control

Basic Physiologic Parameters		Medical	Surgical
Avoid hypoxia and hypercarbia PaO_2 ≥ 11–13 kPa SaO_2 ≥ 97% $PaCO_2$ 4.7–5.3 kPa *Avoid hypotension* CVP ± PAWCP guidance IV fluids, inotropes, vasopressors *Metabolic* Temperature ≤ 37.5° C Normoglycemia Primary neurophysiologic targets ICP ≤ 20 mm Hg CPP ≥ 65 mm Hg *Secondary neurophysiologic targets* $SjvO_2$ 55%–75% $PbtO_2$ ≥ 15 mm Hg	**Early**	Head up (15–30 degrees) Removal of constricting cervical collars—precautions in spinal injury Seizure control Full sedation and muscle paralysis Hyperventilation and ↓ $PaCO_2$ (4–4.5 kPa)—short-term measure only Osmotic diuresis and hyperosmolar therapy: mannitol, hypertonic saline Maintain Na^+ < 155 mmol/L and serum plasma osmolality ≤ 320 mmol/L	Evacuation of significant mass lesions CSF drainage and diversion (external ventricular drainage, or lumbar drainage, if indicated)
	Late	Barbiturate coma Use EEG/BIS monitoring Bolus to achieve burst suppression followed by maintenance infusion Hypothermia (temperature < 35° C)	Decompressive craniectomy

Mannitol is usually given 0.5 to 1 g/kg bolus dosing and usually 20% solution is used. Hypertonic saline has a variety of concentrations including 3%, 5%, and 23.4%. Dose used depends on concentration—2 mL/kg of 5% bolus and 30-mL bolus of 23.4% are examples.
CPP, cerebral perfusion pressure; *CVP,* central venous pressure; *ICP,* intracranial pressure; *PAWCP,* pulmonary artery wedge capillary pressure.

intervention guided by clinical and physiologic parameters. There are early and late strategies, with each containing medical and surgical therapies (Table 26.11).

Late-stage medical measures such as hypothermia and the induction of barbiturate coma do have significant risks associated with them. Barbiturate doses to achieve burst suppression may result in myocardial depression, increased infection risk (especially respiratory), and significant hypotension (vasoactive agents and fluids are required to maintain MAP and CPP). In addition, they have a prolonged $t_{1/2}$, and neurologic assessment may not be possible for a prolonged period.[22] Prophylactic hypothermia should be avoided, and there is debate regarding the timing and degree of hypothermia required for neuroprotection. Hypothermia increases infection risk by suppression of innate immunity and can result in acute kidney injury and reperfusion injury following restoration of normothermia.[23]

The mechanism of action of all interventions to control ICP reflects the manipulation of basic neurophysiologic concepts underpinning intracranial volume and ICP, CBF/CBV, and intracranial compliance:

- Avoidance of hypoxia and hypotension prevents cellular ischemia and edema
- Head up positioning and removal/loosening of cervical collars increases venous outflow: ↓ CBV
- Sedation and hypothermia depress cerebral metabolism, activity, and oxygen consumption with an associated reduction in flow and blood volume: ↓ CBV and CBF
- Paralysis reduces agitation and stress from intubation as well as "fighting" the ventilator (preventing intrathoracic pressure increases and its transmission to cranial cavity with an associated increase in ICP)
- Hyperventilation with ↓ $PaCO_2$ promotes cerebrovascular vasoconstriction: ↓ CBV and CBF
- Hyperosmolar therapy promotes diuresis and decreases vasogenic edema and interstitial edema
- CSF diversion with ventriculostomy or lumbar drainage: ↓ CSF
- Surgical evacuation of mass lesions that contribute additional excess volume within the skull vault
- Decompressive craniectomy: mechanical ↑ in intracranial volume

Treatment of Seizures and Status Epilepticus

Management of seizures and status epilepticus is an important facet in neurosurgical critical care.[24] Any injury to cortical structures theoretically may lower one's threshold for seizure development. A practical classification categorizes seizures into either generalized (tonic, clonic, tonic-clonic, absence) or partial (focal). The latter may be simple, complex (associated with loss of consciousness), or proceed to secondary generalization. Status epilepticus (SE) is defined as ≥ two consecutive seizures without a return to baseline mental status or continuous seizure activity for ≥ 30 minutes. Practically, a seizure lasting ≥ 5 minutes should be considered as SE and treated as such. Nonconvulsive status epilepticus (NCSE) is difficult to diagnose and may only manifest as altered mental status without an apparent etiology.

Clinical Diagnosis

Diagnosis of SE in patients with depressed consciousness level (posttraumatic head injury, intubated and sedated, post

surgery) can be challenging. Systemic physiologic manifestations such as cardiac conditions (tachycardia, hypotension), respiratory conditions (hypoventilation, hypoxia, hypercapnia, aspiration), and pyrexia may be the only markers in the absence of classical neurologic features (altered behavior; mental status; tonic, clonic, or tonic-clonic movements). Unexplained ICP elevation in the absence of significant radiologic abnormality may be another indication.

Etiology and Precipitants

In patients with known epilepsy, the most common cause is noncompliance with antiepileptic drugs (AEDs). Other precipitants (including in those with no prior history) include metabolic abnormalities (electrolyte, glucose, renal or liver failure), drug-related conditions (alcohol, benzodiazepine withdrawal), intracranial lesions (tumor, hemorrhage, stroke, traumatic brain injury), intracranial infection, and iatrogenic post (usually) supratentorial surgery.

Complications

SE is a medical emergency with significant intracranial, systemic (cardiorespiratory), and metabolic consequences. Excessive catecholamine release can result in cardiac arrhythmias and hypotension, increased oxygen consumption, and pulmonary edema. The depression of consciousness level causes hypoventilation, hypoxia, hypercarbia, loss of protective airway reflexes with aspiration risk, and lactic acidosis from increased anaerobic glycolysis. Rhabdomyolysis can compound the acidosis and precipitate renal failure. The excessive neuronal excitotoxicity results in necrosis and apoptosis with mismatch in flow and metabolic demand, cerebral edema, increased ICP, decreased CPP, and ischemia. Mortality of SE in general is approximately 20% and depends on age, duration, and the cause of SE.

Investigation

Once stabilized, any patient with SE should undergo imaging to exclude any intracranial mass lesion as a cause, and this is especially important in patients who were stable neurosurgically and have undergone a deterioration, as it may signify a postsurgical complication (eg, postoperative hemorrhage) or a complication of the patient's pathology (eg, aneurysmal rebleed). EEG is indicated in patients where the diagnosis is uncertain (eg, NCSE) and even following treatment, as a high proportion of patients may still manifest EEG evidence of seizure activity despite the cessation of tonic-clonic activity.

Treatment

Airway protection, maintenance of oxygenation and ventilation, stabilization of hemodynamic parameters, and vascular access are of primary importance. These safeguards are followed by the implementation of pharmacologic therapies in a stepwise escalation, almost all of which can precipitate hypotension and myocardial depression (Table 26.12)[25]:

- First line—ICP–IV bolus phase: benzodiazepines (eg, lorazepam, diazepam, midazolam)
- Second line—IV infusion phase: hydantoins (eg, phenytoin, fosphenytoin)
- Failure of first- and second-line therapies suggests refractory status epilepticus (RSE)
- Third line—anesthetic phase: RSE requires intubation, sedation, and treatment with anesthetic agents including barbiturates (pentobarbital, thiopental, phenobarbital) or hypnotics (eg, propofol, midazolam)
- Doses of third-line agents should be titrated to achieving burst suppression on EEG

The addition of a neuromuscular blockade and muscle paralysis must be considered on an individual basis. Advantages are that it facilitates intubation, decreases ventilatory-associated gag and distress, and reduces the intrathoracic pressures that can occur when a patient "fights" against the ventilator and that may be transmitted intracranially with the resultant elevation in ICP. These must be balanced against the subsequent need for mechanical ventilation, the risks of ventilator-associated complications from prolonged muscle paralysis, respiratory muscle myopathy and critical illness neuropathy, and the possibility that seizure activity may be masked as a result of muscle paralysis.

Infection

It is estimated that for every 1°C change in temperature, the CMR O_2 and CBF can change by as much as ~5% with hyperthermia leading to increased flow and metabolism and thereby elevation in ICP. Fever (temperature ≥ 38°C) in critically ill neurosurgical patients may be due to infection or noninfectious etiologies (Table 26.13). As well as having an impact on ICP (and therefore affecting cerebral perfusion), infection also provides a "second hit" in critically ill patients who may already have dysfunction in one or more organ systems. The risk of systemic physiologic dysregulation and loss of functional reserve leading to a state of multiorgan dysfunction is elevated. Recognition, rapid evaluation, and aggressive treatment with antimicrobials and hemodynamic support are time critical, especially with septic patients where the "golden hour" of treatment is vital for optimal outcomes.

The most common cause for infection in critically ill neurosurgical patients in NCCU is pneumonia.[1] Most of these cases are due to mechanical ventilation, and the risk and rate of infection increase with the duration of mechanical ventilation. Microbes implicated in early infection (with a typical onset of ≤ 3 days following intubation) are usually the same as those associated with community-acquired pneumonia (*Streptococcus pneumoniae, Staphylococcus,* and *Haemophilus influenzae*). Infection following prolonged intubation (with a typical onset of ≥ 3–7 days following intubation) is likely to be due to the common hospital-acquired pathogens (*Pseudomonas aeruginosa,* methicillin-resistant *Staphylococcus aureus*). Another common site is the urinary tract, and this is often associated with the presence of bladder catheterization in critically ill patients. Symptomatic patients should be treated with antibiotics as well as replacement of the likely colonized catheter.

TABLE 26.12 Pharmacologic Aspects of Treatment of Status Epilepticus

	Medication Class	Mechanism of Action	Drug	Loading Dose	Side Effects
First Line: IV Bolus	Benzodiazepines	GABA activity Chloride ion influx Hyperpolarization Inhibition of action potential propagation	Lorazepam Diazepam Midazolam	0.1 mg/kg (max 4–8 mg) Rapid onset (~ 2 mins) 0.15 mg/kg (max 10 mg) High lipid solubility 0.2 mg/kg pH dependent water and lipid solubility (other formulations—intranasal, sublingual—available) but also less responsive as rapid serum clearance	Respiratory depression Hypotension Depressed consciousness level
Second Line: IV Infusion	Hydantoins	↓ Rate of voltage gated Na^+ channel re-opening ↓ Action potential generation and propagation	Phenytoin Fosphenytoin	15–20 mg/kg (rate of infusion 50 mg/min) Therapeutic range (10–20 μg/mL) Water-soluble pro-drug of phenytoin—metabolized by plasma phosphatase 1 mg of phenytoin is equivalent to 1.5 mg of fosphenytoin Loading dose similar to phenytoin	Cardiac dysrhythmias Hypotension Prolongation of cardiac QT interval
Third Line: Anesthetic	Short-acting barbiturates		Pentobarbital	10–15 mg/kg (maintenance rate of infusion 1–3 mg/kg/hour)	Respiratory and myocardial depression
	Benzodiazepines		Midazolam	0.2 mg/kg (maintenance rate of infusion 0.05–2 mg/kg/hour)	Respiratory depression
	Hypnotics		Propofol	1–3 mg/kg (maintenance rate of infusion 1–5 mg/kg/hour)	Hypotension Myocardial depression with sudden cardiovascular collapse Hypertriglyceridemia Metabolic acidosis

TABLE 26.13 Infectious and Noninfectious Causes of Fever in Critically Ill Neurosurgical Patients

Infectious	Noninfectious
• General • Pneumonia (hospital-acquired, ventilator-associated, aspiration due to depressed consciousness level or absence of protective reflexes) • Urinary tract	**General** • Venous thromboembolism (eg, deep venous thrombosis, pulmonary embolism) • Drug induced (eg, antiepileptic, antibiotic induced) • Blood product transfusion reaction
Neurosurgical Specific • Superficial surgical site infection (eg, wound infection) • Deep surgical site infection (eg, intracranial abscess, ventriculitis, bone) • General intracranial infection (eg, meningitis, encephalitis) • External ventricular drain–associated ventriculitis	**Neurosurgical Specific** • "Chemical" meningitis/arachnoiditis (eg, due to blood products irritating cerebrospinal fluid following posterior fossa surgery) • Central hyperthermia often due to hypothalamic dysfunction (eg, post aneurysmal subarachnoid hemorrhage with excessive third ventricular blood load, iatrogenic post surgery near hypothalamic region—pituitary, third ventricular tumor, craniopharyngioma) • Autonomic dysreflexia and autonomic "storms"—characterized by increased sympathetic response (↑ sweating, respiratory secretions, hypertension, tachycardia, tachypnea)

An important consideration specific to critically ill neurosurgical patients is infection in patients with external ventricular drains (EVDs). EVD infection and the associated ventriculitis can pose a considerable burden in patients by increasing mortality and morbidity, prolonging intensive care unit stay, and often necessitating intraventricular antimicrobial administration. The most common microbe implicated is *Staphylococcus*, although in patients with prolonged previous antimicrobial treatment, more virulent and resistant microbes may be involved. There is increasing evidence in the literature that emphasizes the development of "care bundles" in the handling, sampling, and general management of EVDs to reduce overall infection rates (akin to those employed in the care of patients with central venous catheters).[26,27] EVD sampling should be minimized, with the need for EVD sampling and manipulation carefully rationalized; should sampling occur, it should take place using strict aseptic measures and techniques—often in a stringent protocol-driven manner—as both of these strategies have been demonstrated to reduce EVD infection rates.

Electrolyte Disorders

Electrolyte dysfunction following brain injury is commonly encountered in critically ill neurosurgical patients, especially disturbances in sodium and water homeostasis, other electrolytes (potassium, calcium, magnesium, phosphate), and glycemic control. Clinical manifestation is a rapidly evolving interplay of failed homeostatic mechanisms and compensatory physiologic responses as a result of evolutionary metabolic and acute phase responses to stress following brain injury.[28] Management requires an understanding of basic physiologic principles, a regular assessment of clinical and biochemical parameters, and early referral to and expert consultation with nephrologists and endocrinologists to ensure early identification, timely evaluation, and effective management.[29]

Sodium Homeostasis

Sodium (Na^+) is the dominant, most osmotically active extracellular cation, the major contributor to plasma (serum) osmolality (normal range: 285–295 mOsm/L). It regulates water balance and distribution and therefore blood pressure control (distribution between ICF and ECF compartments is osmolality dependent; distribution between the I_{Vasc} and E_{Vasc} spaces of the ECF compartment is dependent on Starling forces) and is involved in the generation of action potentials. Sodium concentration is tightly regulated (135–145 mmol/L) via a complex interplay among afferents, receptors, and efferents involved in the neurohumoral responses that regulate ECF volume, blood pressure, and adjustment of the water content of the ECF via renal mechanisms controlling the excretion of water.

Arginine vasopressin (AVP)—also known as antidiuretic hormone (ADH)—is the principal regulator of total body water and plasma osmolality. Synthesized by the supraoptic and paraventricular nuclei of the magnocellular neurons of the hypothalamus, it is stored in the posterior pituitary and released in response to osmotic (osmoreceptors in the hypothalamus control AVP synthesis and release when serum osmolality rises above 285 mOsm/L) and nonosmotic (reduction in blood pressure and intravascular volume detected by low-pressure baroreceptors in the right atrium and great veins and high-pressure baroreceptors in the carotid sinus) stimuli. It promotes solute free water retention by increasing aquaporin channel insertion of the renal collecting duct with production of concentrated urine and an increased plasma osmolality. Hypotension and hypovolemia also lead to increased sympathetic activity (increased SVR with positive ino- and chronotropic effects), activation of the renin-angiotensin-aldosterone (RAA) axis (the mineralocorticoid function of aldosterone acting as both a vasoconstrictor and a promoter of sodium and water retention at the distal convoluted tubule), and glucocorticoid release (they also promote sodium and water retention). The net effect is to increase circulating volume and blood pressure.

Conversely, atrial natriuretic peptides (ANPs) and brain natriuretic peptides (BNPs) promote natriuresis by increasing renal sodium excretion, inhibiting the RAA axis, reducing brainstem sympathetic outflow, and inhibiting thirst and salt appetite.

Given that sodium and water balance are intricately linked, derangements of sodium are usually associated with derangements of water and vice versa. Hyponatremia (reduced plasma sodium concentration) is related to either water excess or sodium (and secondarily via osmotic pressure, water) depletion. Hypernatremia is due to either water depletion or sodium excess.

Hyponatremia

True hyponatremia (plasma $[Na^+] < 135$ mmol/L) is a serum hypo-osmolar state to be differentiated from artifactual hyponatremia (serum osmolality is usually normal or elevated). Hyponatremia is common in critically ill neurosurgical patients and may occur in the setting of almost any neurosurgical pathologic process, especially in those with TBI, aneurysmal subarachnoid hemorrhage (SAH), brain tumors, infection, and following pituitary surgery, and it may be associated with increased mortality, morbidity, and worse functional outcomes in these settings. It may also be associated with antiepileptic medications (eg, sodium valproate, lamotrigine, carbamazepine). The etiology is diverse and categorized by ECF volume status (Table 26.14), and evaluation and response to treatment require an assessment of ECF status via clinical (cardiac parameters including CVP monitoring, fluid input and urine output charts, consciousness level) and biochemical (serum and urine Na^+ concentration and osmolalities; renal function—urea, creatinine; hematocrit [HCT]; urine dipstick for specific gravity [SG]—low SG < 1.005 suggests dilute urine and high SG > 1.015 suggests concentrated urine; acid-base status) parameters.

Clinical manifestations depend on the severity of hyponatremia and the rapidity of onset. The major complication is cerebral edema from the serum hypo-osmolar state with

TABLE 26.14 Etiology of "True" Hypo-Osmolar (Serum Osmolality < 285 mOsm/L) Hyponatremia Classified by Extracellular Fluid Volume Status

HYPO-volemic		EU/NORMO-Volemic	HYPER-Volemic	
$Urine_{Na+}$ low (<20 mmol/L) → extra renal loss	$Urine_{Na+}$ HIGH (>30 mmol/L) → renal loss	$Urine_{Na+}$ high (>30 mmol/L) $Urine_{Osmolality}$ High	$Urine_{Na+}$ high (>30 mmol/L)	$Urine_{Na+}$ low (<20 mmol/L)
• Skin (burns, cystic fibrosis) • Gastrointestinal (diarrhea, vomiting, intestinal obstruction)	• Adrenal insufficiency • Diuretic use • CSW • Nonoliguric renal failure • Tubulointerstitial disease • DKA	• SIADH • Iatrogenic • Hypothyroidism	• Acute oliguric renal failure	• Cardiac failure • Nephrotic syndrome • Hepatic failure (cirrhosis) • Iatrogenic • Malnutrition • Protein losing enteropathy

CSW, cerebral salt wasting; *DKA,* diabetic ketoacidosis; *SIADH,* syndrome of inappropriate antidiuretic hormone secretion.

TABLE 26.15 Principles Guiding Management of Hyponatremia

Rapidity of correction of serum Na^+	• Patients with minimal symptoms in general require increase by up to 0.5 mmol/L/hour • Maximum increase per day should be 8–10 mmol/L • Severe hyponatremia (<120 mmol/L) or neurologic compromise (eg, seizures), require rapid increases (1–2 mmol/L/hour) over 2–4 hours
Monitoring response to treatment	• Twice daily monitoring of serum Na_+, serum Osm, urine Na_+, and urine Osm with clinical status assessment • Severe hyponatremia or neurologic compromise requires 4–6 hourly assessment
Fluid management depends on extracellular fluid volume status	**HYPO-Volemic** • Cautious rehydration with isotonic crystalloid (0.9% saline) and monitoring to avoid cardiac failure and overload • Severe hyponatremia or neurologic compromise may necessitate hypertonic saline (eg, 1.8%, 3%, 5%) **EU/HYPER-Volemic** • Fluid restriction (750–1000 mL per day) is usually sufficient • Diuresis with diuretics in hypervolemic states may be needed
Additional pharmacologic intervention (with EU- or HYPER-volemic states) Endocrine guidance is recommended in implementation	**Demeclocycline** • Antibiotic impairs and attenuates action of AVP/ADH at renal collecting duct promoting free water excretion **Vasopressor (AVP/ADH) Receptor Antagonists ("Vaptans")** • Promotes free water loss with electrolyte preservation

The effects of a 1 L infusion of intravenous (IV) fluid on serum sodium concentration can be estimated by the following formula: $\Delta\ serum_{Na+} = (infusate_{Na+} - serum_{Na+})/(TBW + 1)$. This formula assumes no loss of sodium or water from the body and no other gain in sodium or water during the infusion period.
AVP/ADH, arginine vasopressin/anti-diuretic hormone; $\Delta\ serum_{Na+}$, estimated change in serum sodium concentration; $infusate_{Na+}$, sodium concentration within the IV fluid; $serum_{Na+}$, current measured serum sodium concentration; TBW, total body water in liters.

neurologic features that include headache, lethargy, altered mental status, seizures, brainstem herniation, and cardiorespiratory arrest. A diagnostic schema for the assessment of hyponatremia should address the following questions:

- What is the serum osmolality ($serum_{Osm}$)?
  - Low $serum_{Osm}$ (< 285 mOsm/L) → true hypo-osmolar hyponatremia
  - Normal or high $serum_{Osm}$ (> 295 mOsm/L) → artifactual hyponatremia
- If true hypo-osmolar hyponatremia, what is the extracellular fluid (ECF) volume status?
  - HYPO-volemic (dehydration)
  - EU/NORMO-volemic
  - HYPER-volemic (edema, fluid overload)
  - What is the urinary sodium concentration ($urine_{Na+}$) and urinary osmolality ($urine_{Osm}$)?

Treatment principles are to restore serum sodium and correct the etiologic factor (Table 26.15). The need for and

rapidity of correction depend on the presence or absence of neurologic compromise as a result of hyponatremia, the chronicity of the condition, the rate at which it has developed, and the extracellular volume status. Overly rapid correction must be avoided, as it can precipitate central pontine myelinolysis (CPM), an irreversible and often fatal pontine demyelination syndrome presenting with features of lethargy, pseudobulbar palsy, quadriparesis, and death. Treatment of symptomatic hyponatremia is targeted to the point of alleviation of symptoms rather than to an arbitrary serum sodium value and should be monitored and managed in the NCCU to minimize the risk of overly rapid sodium correction.

Syndrome of Inappropriate Antidiuretic Hormone Secretion (and Cerebral Salt Wasting)

Two common causes of hyponatremia in critically ill neurosurgical patients are syndrome of inappropriate ADH secretion (SIADH) (often, though not exclusively, seen in the setting of tumors and trauma) and cerebral salt wasting (CSW) (often, though not exclusively, seen in the setting of aneurysmal SAH). Both manifest with a hypo-osmolar hyponatremia with inappropriately high urine sodium concentration. The key parameter that helps to differentiate between the two is intravascular and extracellular fluid volume status (Table 26.16): SIADH is a volume replete (EU-volemic) state, whereas CSW is a volume-depleted (HYPO-volemic) condition. Management is radically different.

The pathophysiology of SIADH is an excessive, inappropriate release of AVP/ADH by either a pituitary or an ectopic source and occurs in the absence of the normal stimuli for its release. Acute neurologic injury (eg, intracranial infection, TBI, aneurysmal SAH, intracranial hemorrhage, malignancy, venous thrombosis, following pituitary surgery), systemic malignancy (eg, small cell lung carcinoma precipitating a paraneoplastic syndrome with ectopic ADH secretion), drugs (eg, antiepileptics, antipsychotics, antidepressants) and pulmonary pathology (eg, pneumonia, tuberculosis, and pulmonary abscesses) can all cause SIADH. The diagnosis requires certain criteria to be fulfilled (Table 26.17).

Electrolyte-free water restriction is usually the mainstay of treatment for SIADH resulting in a slow rise in serum sodium of 1.5 mmol/L/day. However, this is often contraindicated in critically ill neurosurgical patients for whom fluid restriction may worsen cardiovascular instability and the risk of cerebral ischemia (eg, aneurysmal SAH). An infusion of hypertonic saline may be indicated in these circumstances. Pharmacologic options include the use of demeclocycline and "vaptans" under expert endocrinologic guidance.

CSW is a state of impaired renal sodium reabsorption and primary natriuresis resulting in a hypo-osmolar hyponatremia with severe hypovolemia and intravascular volume depletion. It is commonly seen following aneurysmal SAH. The pathophysiology is likely to be related to a systemic release of natriuretic factors (ANP, BNP), impaired sympathetic renal input, or both. Management is volume repletion with isotonic crystalloid, although hypertonic solutions may be required. Fludrocortisone—a synthetic mineralocorticoid—increases sodium reabsorption from renal tubules and may be used to attenuate sodium and water loss in CSW.

Hypernatremia

Hypernatremia (plasma [Na^+] > 145 mmol/L) may be secondary to either water (hypotonic fluid) depletion or sodium (solute) excess (Table 26.18). Clinical manifestations are similar to those of hyponatremia. Management involves correction of the etiologic factor and, if the primary deficit is water

TABLE 26.16 Differentiating Between Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and Cerebral Salt Wasting (CSW)

	SIADH	CSW
Serum Na^+	LOW	LOW
Extracellular Volume Status	EU- or NORMO-volemic	HYPO-volemic
Urine Na^+	High (>25 mmol/L)	Very high (>40 mmol/L)
Urine Osmolality	High (solute free water retention with hyperosmolar concentrated urine)	High (excessive natriuresis in urine with hyperosmolar concentrated urine)
Hematocrit	Normal	High
Urea/Creatinine Ratio	Normal or Low	High

Laboratory and biochemical markers are often unreliable, and the most reliable critical parameter is the clinical assessment of extracellular fluid volume status.

TABLE 26.17 Diagnostic Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

- Hypo-osmolar hyponatremia (serum Osm < 285 mOsm/L and serum Na^+ < 135 mmol/L)
- Normovolemic extracellular volume status
- Normal renal, thyroid and adrenal function
- "Inappropriate" high urine osmolality (ie, urine that is not maximally diluted)
- "Inappropriate" high urine sodium excretion (urine Na+ > 30 mmol/L)
- Improvement in symptoms and serum sodium with fluid restriction

When encountered with urine and serum osmolalities and a diagnosis of SIADH is considered, an important principle to emphasize is that there are no fixed thresholds. In the right clinical context and provided other criteria are satisfied, as long as serum osmolality is low (ie, $serum_{Osm}$ < 285 mOsm/L) and urine osmolality is high (ie, urine is not maximally dilute—usually $urine_{Osm}$ > 100 to 150 mOsm/L), a diagnosis of SIADH can be made clinically.

TABLE 26.18 Causes of Hypernatremia

Free Water Depletion (Hypotonic Fluid Loss)	Sodium (Solute) Excess
Renal Loss • Diabetes insipidus (cranial or nephrogenic) • Osmotic (eg, hyperglycemia in diabetic ketoacidosis)	**Iatrogenic** • Excess IV hydration with sodium rich fluids • Hyperaldosteronism with renal retention
Inadequate Intake • Dehydration • Inadequate oral intake due to depressed consciousness level	**Primary** • Conn syndrome (aldosterone secreting neoplasm in adrenal gland) • Cushing syndrome (glucocorticoid excess, which has some mineralocorticoid activity)
Skin Loss • Burns • Fever and excessive sweating	**Secondary (Relative Renal Hypoperfusion Precipitating Activity of the Renin-Angiotensin-Aldosterone Axis)** • Cardiac failure • Liver failure • Renal failure
Gastrointestinal Loss • Vomiting • Diarrhea • Nasogastric suction	
Respiratory Loss • Hyperventilation	

TABLE 26.19 Causes of Cranial or "Central" Diabetes Insipidus

Trauma	Post elective or emergency pituitary surgery TBI (DI may be temporary if trauma is distal to pituitary stalk as proximal nerve endings can reinnervate sites of ADH secretion)
Neoplastic	Pituitary adenoma or carcinoma Craniopharyngioma Metastatic Hypothalamic glial tumor
Vascular	Pituitary hemorrhage and infarction (eg, Sheehan syndrome with acute pituitary infarction from hypovolemic shock) Post aneurysmal SAH
Inflammation	Sarcoidosis
Infection	Meningitis Intracranial abscess Encephalitis
Congenital	Defects in genes regulating ADH (eg, Wolfram syndrome—autosomal recessive, characterized by DI, diabetes mellitus, optic atrophy, and deafness)

TBI, Traumatic Brain Injury; *DI,* Diabetes insipidus; *ADH,* Anti-Diuretic Hormone; *SAH,* subarachnoid haemorrhage.

depletion, replacing the deficit with oral (enteral) water or relatively hypotonic IV fluids. In critically ill neurosurgical patients, hypotonic solutions (eg, 5% dextrose) are avoided due to the concern of precipitating cerebral edema. Cautious rehydration with isotonic crystalloid (0.9% saline) to correct the volume depletion will correct the plasma sodium concentration. Salt and fluid restriction is considered in the setting of solute excess.

Diabetes Insipidus

Diabetes insipidus (DI) is a pathologic syndrome resulting from the failure of AVP/ADH homeostasis leading to loss of urinary concentrating ability, solute-free water excretion, polyuria, dehydration, hypernatremia, and serum hyper-osmolality. DI is categorized as either cranial/central (dysfunction of the hypothalamo-pituitary axis with failed production of AVP; Table 26.19) or nephrogenic (insensitivity of the renal system to the effects of AVP secondary to genetic, metabolic, and drug-induced causes). The most commonly encountered form in critically ill neurosurgical patients is cranial/central DI, and it usually occurs following pituitary surgery/apoplexy or severe TBI.

DI is characterized by thirst, severe polyuria (> 3 L/day), and compensatory polydipsia in alert patients with intact thirst mechanisms. In critically ill neurosurgical patients with blunted sensorium and thirst mechanisms without access to hypotonic fluids, or in those unable to keep up with polyuria, severe dehydration, hypernatremia (serum Na^+ > 145 mmol/L), serum hyperosmolality ($serum_{Osm}$ > 295 mmol/L), and inappropriately dilute urine ($urine_{Osm}$ < 350 mmol/L and urine SG < 1.005) occurs. Other electrolyte derangements (eg, hypokalemia, hypomagnesemia, and hypophosphatemia) may accompany the severe polyuria and also require correction.

The water deprivation test evaluates renal concentrating ability assisting in the diagnosis of DI; in normal individuals (or primary polydipsia), water deprivation stimulates AVP production with decreased urine output, production of concentrated urine, and increased urine osmolality. In true DI, the lack of AVP production means that urine osmolality remains low. The safety and utility of performing such tests in critically ill neurosurgical patients, however, are questionable given its ability to cause further hypovolemia and hemodynamic instability. In most neurosurgical patients (especially those following pituitary surgery), a pragmatic approach to the diagnosis of cranial DI is taken, with the diagnosis confirmed in the appropriate clinical context with supportive evidence from the following parameters: polyuria (> 250 mL/hour for 3 consecutive hours or > 750 mL over 3 hours), hypernatremia, and dilute urine.

Treatment involves correction of the hyperosmolar state and restoration of intravascular volume. The correction should not exceed 1 to 2 mmol/L/hour or 8 to 10 mmol/L/day. Alert patients with intact thirst and tolerance of enteral replacement should be encouraged to "drink to thirst" with oral water. This is usually sufficient to replace the deficit in mild DI. In unconscious patients, titrated enteral (nasogastric) replacement may

be required. In those with severe polyuria and severe DI or those unable to drink, the administration of desmopressin (DDAVP)—a synthetic V_2 receptor agonist and two-amino acid substitute for AVP/ADH—may be administered either intravenously or subcutaneously (0.5–1 μg).

Disturbances of Other Electrolytes

A variety of other electrolyte disturbances may occur in critically ill neurosurgical patients including those involving potassium, calcium, magnesium, and phosphate. The etiology is complex and multifactorial with dysfunction in endocrine organs controlling electrolyte and fluid concentration occurring as a specific consequence of brain injury, a systemic dysregulation in the context of multiorgan failure (MOF) in critically ill patients, or iatrogenically due to the administration of incorrect electrolyte or fluid volumes. Early identification and expert management are critical due to the multisystemic nature of complications that may arise, including those of a cardiovascular (eg, circulatory collapse, arrhythmias) or neurologic (eg, seizures, coma) nature. Phosphate disorders may, for example, precipitate diffuse neuromuscular weakness with respiratory failure.

Glycemic Control

Benefits of strict glycemic control have been demonstrated in a prospective randomized control trial in critically ill patients in a general critical care setting.[30] However, some studies have also illustrated the possible negative impact of applying such stringent glycemic ranges, chief among them being the risk of clinically significant hypoglycemic events. As well as debate regarding the most appropriate "normoglycemic" range that balances the benefits of glycemic control against the risks of hypoglycemia, there is a degree of uncertainty as to whether results from studies in general medical or surgical intensive care units are applicable en bloc to a neurocritical care setting. Brain metabolism is highly dependent on a constant glucose supply. Patients with acute brain injury have a heightened susceptibility to the effects of hyper- or hypoglycemia. Even modest hypoglycemia may trigger states of energy failure and metabolic crises, whereas the deleterious effects of hyperglycemia in lowering the ischemic neuronal threshold, destabilization of blood-brain barrier, increased development of cerebral edema, increased acidosis from anaerobic glycolysis, and free radical–mediated injury are well documented.

Hyperglycemia has been shown to be associated with adverse outcomes in a variety of neurosurgical conditions. A meta-analysis confirmed an association between hyperglycemia and poor clinical outcome following aneurysmal SAH with an increased risk of death and disability, pneumonia, cerebral edema, and delayed cerebral ischemia. In patients with intracerebral hemorrhage (ICH), both diabetic patients and nondiabetic patients with admission hyperglycemia were at a higher risk of having a poor outcome. An increase in blood glucose concentration of 1 mmol/L has been associated with a 33% increase in early mortality with a cutoff glucose concentration for optimal outcome prediction of 9.1 mmol/L.

These findings certainly mirror that observed in the setting of severe TBI, where several studies have demonstrated that although hyperglycemia should clearly be avoided, the optimal target glucose range is yet to be determined with an absolute need to avoid the deleterious effects of hypoglycemia. Based on current evidence, the risks of intensive insulin therapy (IIT: 4.4–6.7 mmol/L) in TBI appear to outweigh the benefits, and intermediate- or moderate-level glucose control (6–10 mmol/L) appears optimal to avoid both hyper- and hypoglycemic extremes.[31]

Venous Thromboembolism

Venous thromboembolism (VTE) is a common complication in critically ill neurosurgical patients and may manifest as either deep venous thrombosis (DVT) or a more life-threatening pulmonary embolism (PE). It is especially common in patients with traumatic brain injury and spinal cord injury (due to prolonged immobility) and patients with intracranial malignancy (hypothesized as due to a pro-coagulopathic state). Mechanisms of prophylaxis include mechanical (eg, graduated thromboembolic deterrent compression stockings, intermittent pneumatic compression devices) and chemical (eg, unfractionated heparin or fractionated low-molecular-weight-heparin—enoxaparin). Decisions with regard to the timing of the initiation of pharmacologic VTE prophylaxis should be made on an individual basis by risk-benefit analysis and stratification.[32] In special circumstances when patients have been on lifelong anticoagulation due to preexisting conditions (eg, recurrent DVT or PE, metallic heart valves) and present with life-threatening intracranial hemorrhage, spinal injury, or an intracranial pathology that requires high-risk surgical intervention, expert guidance should be sought with regard to issues such as stopping anticoagulation, temporizing measures such as bridging anticoagulant therapy or inferior vena caval filters, and timing of the reinitiation of anticoagulation.

Management of Specific Neurosurgical Pathology

It is beyond the scope of this chapter to provide detailed reviews on the specifics of each neurosurgical pathologic process. This short section summarizes the critical nuances that may be encountered with the common neurosurgical pathologies in critically ill neurosurgical patients.

Traumatic Brain Injury

The pathophysiology of traumatic brain injury (TBI) is so heterogeneous that development of a single therapeutic paradigm to encompass all patients and scenarios is inherently difficult. The principal aim of management is to limit and prevent secondary brain injury by maintaining cerebral perfusion, preventing hypotension (SBP < 90 mm Hg) and hypoxia (PaO_2 < 60 mm Hg or 8 kPa)—both of which independently contribute to an increased risk of mortality and worse

outcome—and averting other systemic metabolic and physiologic derangements. A significant number of the principles regarding multimodality monitoring in critically ill neurosurgical patients, therapeutic targets regarding ICP and CPP, and other aspects of management (eg, protocol-driven step-by-step escalation therapeutic paradigms for treatment of raised ICP) have derived from research into managing TBI patients. The updated Brain Trauma Foundation guidance forms a detailed review on the management of traumatic brain injury patients including critical care management.[33] The general principles and aims described throughout this chapter apply, and the overarching aims include the following:

- Apply a multimodal approach to neurologic monitoring in order to optimize physiology, facilitate the early identification and treatment of secondary insults, and individualize therapy
- Maintain optimal CPP and ICP targets, including advanced monitoring targets (eg, $SjvO_2$ and $PbtO_2$)
- Employ a stepwise escalation of therapies for ICP control to be implemented early

Vascular Pathology

Spontaneous intracranial hemorrhage usually occurs in the subarachnoid space secondary to aneurysmal rupture or in the cerebral or cerebellar parenchyma, secondary to either a vascular lesion (eg, aneurysm, arteriovenous malformation [AVM]) or other etiologies (eg, hypertension, anticoagulant use, amyloid angiopathy, drug use). Each pathologic process has specific nuances that need to be considered. General aspects of care in all patients with spontaneous intracranial hemorrhage include stringent control of blood pressure with targets varying between normotension and hypertension depending on clinical goal, adequate sedation if patients are on mechanical ventilation to avoid spikes in ICP secondary to agitation or ventilator dyssynchrony, VTE prophylaxis, and control of hyperglycemia.

Aneurysmal rupture with bleeding into the subarachnoid space results in an intense systemic catecholamine surge in conjunction with sympathetic activation that precipitates a variety of systemic complications in conjunction with the neurologic insults that need careful observation for treatment in the NCCU in the first 2 weeks following the ictus (Table 26.20). Blood pressure control following aneurysmal SAH represents a challenge. The relationship between blood pressure and rebleeding risk in unsecured aneurysms has not been fully established with some studies suggesting an increased risk of rebleeding with systolic blood pressure > 160 mm Hg. In the presence of unsecured aneurysms, most neurosurgeons would aim for SBP ≤ 140 mm Hg and MAP ≤ 90 mm Hg.

Following surgical treatment of vascular lesions, blood pressure should be carefully monitored. Perioperatively, during AVM surgery in particular, blood pressure targets balance the aim of reducing intraoperative blood loss and hemorrhage against maintenance of cerebral perfusion to avoid ischemia. As a consequence, in the immediate postoperative phase, patients are at risk of developing hyperemic or normal pressure perfusion breakthrough complications such as cerebral edema or postoperative hemorrhage. If patients are kept sedated following surgery, ICP monitoring is often indicated.

Patients with cerebellar hemorrhages should have a lower threshold for intervention due to the small volume of the posterior fossa and high risk of brainstem compression even with small hematomas. The indication for surgical intervention is dependent on hematoma size, the degree of brainstem compression, and the degree of fourth ventricular effacement. Patients being managed with CSF diversion (EVD insertion) require intense monitoring, as blockage may precipitate rapid deterioration with hydrocephalus.

Brain Tumors

Patients undergoing surgery for any intracranial lesion require monitoring in a high-dependency unit in the immediate postoperative phase. Complications include postoperative hemorrhage, iatrogenic ischemia and infarction secondary to arterial or cortical/dural venous sinus thrombosis and occlusion, seizures and status epilepticus, pneumocephalus, malignant cerebral edema, and hydrocephalus. Following brain tumor surgery, most patients continue with high-dose dexamethasone in the first 48 hours, after which they are rapidly weaned. A clear tapering plan with neuro-oncologists must be in place for patients with brain tumors who are receiving steroids postoperatively to avoid steroid-related complications.

Posterior Fossa Surgery

Patients undergoing posterior fossa surgery require careful postoperative care and vigilance. Lesions within the fourth ventricle or cerebellopontine angle are within the vicinity of critical brainstem structures regulating cardiorespiratory function, airway protection, swallowing, and consciousness. Patients should be carefully monitored for postoperative difficulties with swallowing, adequacy of vocal cord function, and airway protection to avoid aspiration (early assessment by speech and language therapists, enteral supplementation via nasogastric feeding). Postoperative hematomas may directly compress lower brainstem structures, leading to rapid deterioration with cardiorespiratory compromise (eg, cardiac arrhythmias, Cushing reflex) without classical features of transtentorial uncal herniation. Dysfunction of cerebrospinal fluid pathways may occur with the presence of acute hydrocephalus, which may necessitate external ventricular drain insertion. Patients require monitoring for chemical meningitis, which frequently occurs following posterior fossa surgery (and requires treatment with serial lumbar punctures and a short course of dexamethasone once the infection has been excluded).

Pituitary Surgery

Patients undergoing pituitary surgery may have features of hormonal hyper- or hyposecretion requiring careful preoperative assessment and optimization. Pituitary apoplexy may

TABLE 26.20 Neurologic and Systemic Complications Following Aneurysmal Subarachnoid Hemorrhage

Site	Complication	Management
Cranial	Ictus	Acute ↑ ICP secondary to hematoma, cerebral edema or acute obstruction of CSF pathways with hydrocephalus: surgical decompression or CSF diversion
	Rebleeding	Definitive treatment for aneurysm to reduce risk of hemorrhage and associated mortality and morbidity: microsurgical or endovascular intervention
	Vasospasm	Serial neurologic examination for any deterioration, monitor with transcranial Doppler and CT perfusion/angiography: nimodipine as primary prophylaxis (improves overall outcome); medical intervention classically involves triple "H" therapy (hypertension, hypervolemia, and hemodilution); in practice adequate normovolemia and hypertension are critical; endovascular intervention may be required in certain circumstances
	Hydrocephalus	Careful observation for hydrocephalus; risk is increased with intraventricular hemorrhage: external ventricular drainage or lumbar drainage (if no contraindication) of CSF, long-term shunting may be required
	Seizures	Role of primary prophylaxis is controversial: if seizures manifest, treatment with antiepileptic medication recommended
	Electrolyte—Na^+ dysfunction	Hyponatremia is common; SIADH and CSW may both occur; fluid restriction is contraindicated following SAH due to risk of hypovolemia and vasospasm precipitation: treat appropriately but avoid fluid restriction in SIADH
Cardiac	Dysrhythmias	Monitor electrolytes: advanced cardiac life support algorithms to manage
	Myocardial injury	Monitor cardiac enzymes (eg, troponin): invasive monitoring with PAFC for management of SVR, CO, and PAWCP; inotropic support
	Hemodynamic control	Prior to definitive treatment of aneurysm, cautious approach to blood pressure control; in general, patient should be allowed to autoregulate to his or her normal pressure, avoiding extremes; after securing aneurysm, aggressive hypertension if vasospasm
Pulmonary	Edema	Edema may be secondary to cardiac failure or neurogenic pulmonary edema: ECHO for diagnosis, oxygen, ventilatory support, diuresis
	Aspiration/ pneumonia	Depressed consciousness level and prolonged intubation increase risk of aspiration and development of ventilator-associated complications (eg, pneumonia): aim to extubate as quickly as possible, aggressive treatment of infection with antimicrobials

ICP, Intracranial pressure; *CSF,* cerebrospinal fluid; *SIADH,* Syndrome of Inappropriate ADH secretion; *CSW,* Cerebral salt wasting; *PAFC,* Pulmonary artery flotation catheter; *SVR,* Systemic vascular resistance; *CO,* cardiac output; *PAWCP,* Pulmonary artery wedge capillary pressure; *ECHO,* echocardiography.

present with severe dehydration and features of hypocortisolism requiring steroid replacement, fluid replacement, and electrolyte correction. Panhypopituitarism may be also be a complication iatrogenically post surgery and in the immediate postoperative phase,[34] patients are started on steroid replacement with hydrocortisone until there has been a formal endocrine evaluation of their hypothalamic-pituitary-organ axes. Steroid doses should be increased during "stress" periods (eg, infection). The most common complication is salt and water balance dysfunction (transient DI causes hypernatremia; the most common cause of hyponatremia is SIADH or perioperative fluid excess, although CSW may occur). Treatment involves an assessment of serum/urine osmolality, urinary sodium and urine specific gravity, and fluid balance management. In patients with DI associated with complications (excessive polyuria, hypernatremia), DDAVP replacement is indicated. Other complications are rare, but patients should be monitored for signs of CSF leakage, pneumocephalus precipitating seizures (which suggest inadequate dural reconstruction or may occur following placement of lumbar drainage for CSF diversion to protect skull base reconstruction), and postoperative hematomas (commonly secondary to persistent venous ooze from cavernous sinuses).

Neuromodulation and Epilepsy Surgery

Patients undergoing neuromodulation (eg, insertion of deep brain stimulation for Parkinson disease) and epilepsy surgery have complex preoperative medication regimens, and it is essential for these to continue during the postoperative phase in consultation with the treating neurologist. Patients with Parkinson disease in particular may manifest with significant dyskinesias or lose regulation of their on/off periods if medication is missed, resulting in significant emotional and physical morbidity. In patients undergoing epilepsy surgery, the risk of seizures including progression to status epilepticus is increased, especially in the immediate postoperative phase, and may be precipitated by a postoperative complication (eg, hemorrhage)

or metabolic changes, drugs (eg, local anesthetic toxicity), or hypercapnia.

Spinal Cord Injury

The primary injury to the spinal cord following a pathologic process (eg, trauma, hemorrhage) may be exacerbated by secondary injury due to systemic factors (eg, hypotension, hypoxia). Spinal shock is characterized by flaccid paralysis and occurs immediately following spinal cord injury due to a loss of somatic and visceral sensory and motor function and of somatic and autonomic reflexes. Depending on the level of injury, cardiac and respiratory function may also be compromised.

Injuries at the lower cervical or thoracic level may disrupt both cardiac function and sympathetic outflow. The resultant loss of sympathetic tone with unopposed parasympathetic activity manifests as bradycardia (due to a loss of cardiac chronotropic activity) and hypotension (due to a loss of cardiac inotropic activity, a loss of vasoconstrictive function with systemic vasodilation, and a loss of systemic vascular resistance as well as the associated vascular leakage and third space fluid loss with hypovolemia). This is termed *neurogenic shock* and impairs perfusion of an already compromised spinal cord. The presence of associated injuries with acute blood loss (eg, pelvic fractures) may result in true hypovolemic shock and further exacerbate the primary spinal cord injury.

High cervical lesions (C3–C5 is the outflow for diaphragmatic muscle control) can result in diaphragmatic, intercostal, and accessory muscle paralysis with ventilatory dysfunction and exacerbate hypoxia. Alveolar ventilation and vital capacity may also be reduced together with the effectiveness of cough mechanisms to clear secretions. The risk of aspiration and infective pulmonary complications therefore increases. The presence of concomitant pulmonary lesions (eg, lung contusions, hemothorax) further compounds the injury. Table 26.21 summarizes critical aspects of care to consider when managing the patient with spinal cord injury.

A special consideration is to reduce the risk and minimize the impact of autonomic dysreflexia and its associated sympathetic surges and hypertensive crises. Precipitant stimuli (eg, pain, gastric distention, urinary retention, constipation) should be managed aggressively; the approach should include adequate analgesia and pain control, consideration of nasogastric tube insertion for gastric decompression of gastric atony and paralytic ileus that may occur following autonomic dysfunction, and urinary catheterization to treat bladder atony and urinary retention. Patients should be referred early to physicians who specialize in spinal cord injury rehabilitation to optimize their care and management.[35]

Brain Death

The definition and diagnosis of brain death vary throughout the world.[36] Conceptually, it is the irreversible loss of cerebral and brainstem function confirmed by the absence of specific physiologic responses and reflexes. Severe brain injury should not be synonymous with brain death; however, the diagnosis of brainstem death allows for the discontinuation of futile treatment. It is highly recommended that specific national, regional, and institutional guidelines be adhered to when the diagnosis is confirmed.

TABLE 26.21 Aspects of Care in Patients With Spinal Cord Injury

Initial Assessment	Cervical spine immobilization as per Advanced Trauma Life Support guidelines Full logroll and spinal boards for transfers
Airway and Breathing	Intubation with minimal spinal cord manipulation if any concerns over airway patency exist (eg, aspiration, high cervical injury, acute lung injury) Awake fiberoptic intubation, manual inline immobilization of spine
Cardiovascular	Avoidance and aggressive treatment of hypotension Spinal cord perfusion may be considered akin to cerebral perfusion Judicious fluid input to avoid hypovolemia guided by invasive monitoring (avoid vasodilation-associated capillary leakage and pulmonary edema) Vasopressor/inotropic support to augment loss of sympathetic tone may be needed
Spinal Precautions and Positioning	Care with transfers—logroll for cervical spine injuries Cervical collars to be relaxed if risk of aspiration or for intracranial pressure control purposes Positioning balances need for optimal spinal cord perfusion (flat bed rest) versus risk of airway aspiration and ventilation (reverse Trendelenburg)
Avoidance of Pressure Ulceration	Regular turning to avoid pressure ulceration (especially over sacrum) Remove spinal boards as soon as possible Cervical collars should have adequate padding
VTE Prophylaxis	Mechanical (graduated thromboelastic stockings; intermittent pneumatic compression devices) and pharmacologic (eg, low-molecular-weight heparin) prophylaxis should be instituted (if no contraindication)
Steroids	Controversial with some evidence for benefits but also risk of complications

The diagnosis of brain death relies on the application of the following concepts:

1. Clinical examination
   a. Confirmation of irreversible coma state
   b. Confirmation of the etiologic cause
   c. Exclusion of any reversible causes
   d. Brainstem function testing to confirm the diagnosis of brainstem death
2. Adjunctive tests—used to support the diagnosis of brain death and include EEG and auditory brainstem evoked potentials
3. Confirmatory tests—used to confirm the diagnosis of brain death by demonstrating an absence of cerebral blood flow and perfusion and thus nonviability of the brain; tests include cerebral angiography, transcranial Doppler (TCD) sonography, and nuclear imaging

Clinical Examination

An irreversible coma state means the patient must be totally unresponsive (including an absence of seizures and limb movements, with the exception of spinal reflexes) and ventilator dependent. The etiologic cause must also be confirmed. Prior to the commencement of brainstem function testing, all reversible causes must be excluded. Brainstem function testing is then performed to confirm the diagnosis of brainstem death by demonstrating the loss of function in all brainstem reflexes. Loss of function usually occurs in a rostral-to-caudal direction in the brainstem: midbrain (cranial nerve III), pontine (cranial nerves V, VII, and VIII), and medulla (cranial nerves IX and X) (Table 26.22).

Adjunctive Tests

EEG is used to confirm the absence of cortical activity or function (absence of activity > 2 mV for > 30 minutes) and to verify that auditory brainstem evoked potentials are absent when all of the waves are absent except the first wave generated by cranial nerve VIII.

Confirmatory Tests

These tests confirm the diagnosis by demonstrating the absence of cerebral blood flow and perfusion thereby providing evidence of the nonviability of cerebral tissue. Cerebral angiography is the gold standard but is invasive, whereas TCD is noninvasive but operator dependent.

TABLE 26.22 Clinical Criteria for Diagnosis of Brainstem Death

Exclusion of reversible factors	1. Hypotension 2. Electrolyte, acid-base or endocrine dysfunction 3. Hypothermia (core temperature < 35°C) 4. Drug-induced central nervous system depression with associated loss of brainstem reflexes and isoelectric EEG (eg, neuromuscular blockage, barbiturates, opioids, volatile anesthetics, benzodiazepines, toxicology screening) 5. Mimics (eg, "locked-in syndrome" secondary to ventral pontine infarction; Guillain-Barré syndrome)	
Brainstem Function Testing		
	Cranial Nerves Assessed	**Response to Testing**
Pupillary light reflex	II (Afferent) III (Efferent)	Pupils are fixed, dilated, and not responsive to light
Corneal reflex	V (Afferent) VII (Efferent)	Absence of corneal reflexes bilaterally
Facial grimace response to painful stimulus	V (Afferent) VII (Efferent)	Absence of facial grimace response to supraorbital ridge/nailbed pressure
Vestibulo-ocular reflex (VOR)	VIII (Afferent) III and VI (Efferent)	Absence of normal "doll's-eye" reflex
Oculocephalic reflex	VIII (Afferent) III and VI (Efferent)	Irrigation with 20 mL of iced water into tympanic membrane normally results in ocular deviation to the opposite side; this reflex is absent in brainstem death
Palatal gag and cough reflex	IX (Afferent) X (Efferent)	Cough or gag reflex to suctioning
Apnea test	Activation of brainstem respiratory center secondary to chemoreceptor triggering following respiratory acidosis	Patient preoxygenated for 10 minutes with 100% O_2 (FiO_2 = 1); ventilator is disconnected with supplemental O_2 supplied by T-piece/suction catheter (6 L/min); hemodynamic stability is ensured; apnea test is positive if there is no triggering of respiratory effort when $PaCO_2$ > 60 mm Hg or > 20 mm Hg rise from normal baseline

Variation in Requirements

Variability exists in different countries with regard to the number of observers required to confirm the diagnosis, the specialty, the duration since primary medical qualification of the observers, the duration of observation, and the use of adjunctive or confirmatory testing. In the United Kingdom, two doctors who have been qualified for at least 5 years must perform brainstem death testing, and they should ideally be professionals involved in the care of neurologically critically ill patients. These specialists include intensivists, neurosurgeons, or neurologic physicians; they should not be members of the organ retrieval or transplantation service. In the United States,[37] the diagnosis of brain death requires a demonstration of the irreversible cessation of function of the entire brain including the brainstem. Clinical examination is usually insufficient on its own. Adjunctive and confirmatory tests are required. In the UK, clinical examination to demonstrate brainstem death together with a clear diagnosis of severe brain injury is sufficient, and adjunctive and confirmatory testing is often not required. The use of confirmatory testing is, however, recommended in some countries for children < 1 year.[38]

Conclusion

The principal concept in the management of critically ill neurosurgical patients is to maintain cerebral perfusion, avoid cerebral ischemia, and limit the impact of secondary brain or spinal injury due to systemic and metabolic derangements. Understanding the relevant neurophysiologic principles governing cerebral blood flow, cerebrovascular autoregulation, cerebral perfusion pressure, and intracranial pressure is the key to strategizing the application of various interventional therapeutic modalities designed to manipulate these aforementioned parameters in critically ill neurosurgical patients. A systematic and methodical approach should be applied in the assessment and evaluation of critically ill neurosurgical patients to enable early identification of etiologies for deterioration, appropriate investigation, and early escalation and implementation of intervention. Neurologic monitoring is an important tool in caring for critically ill neurosurgical patients. The concept of multimodal monitoring individualizes therapeutic regimens, but it is important to remember that trends and variability over a time course provide more useful information than isolated measurements, and their interpretation should be in the context of a clinical assessment of the patient. Complications common to all critically ill neurosurgical patients include intractable elevation in ICP, seizures and status epilepticus, electrolyte dysfunction (especially sodium), and infection; a structured approach to assessment, investigation, and management of each complication is essential. Each neurosurgical pathologic process has its own unique nuances, which should be borne in mind when managing the condition in critically ill neurosurgical patients. Finally, the diagnosis of brain death and therefore the futility of continuing treatment is an important part of managing critically ill neurosurgical patients. Familiarity with international, regional, and institutional guidelines and their application is vital.

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