Critical Care Management of Increased Intracranial Pressure

Stephan A. Mayer, MD*† and Ji Y. Chong, MD*

Increased intracranial pressure (ICP) is a pathologic state common to a variety of serious neurologic conditions, all of which are characterized by the addition of volume to the intracranial vault. Hence all ICP therapies are directed toward reducing intracranial volume. Elevated ICP can lead to brain damage or death by two principle mechanisms: (1) global hypoxic-ischemic injury, which results from reduction of cerebral perfusion pressure (CPP) and cerebral blood flow, and (2) mechanical compression, displacement, and herniation of brain tissue, which results from mass effect associated with compartmentalized ICP gradients. In unmonitored patients with acute neurologic deterioration, head elevation (30 degrees), hyperventilation (pCO2 26–30 mmHg), and mannitol (1.0–1.5 g/kg) can lower ICP within minutes. Fluid-coupled ventricular catheters and intraparenchymal pressure transducers are the most accurate and reliable devices for measuring ICP in the intensive care unit (ICU) setting. In a monitored patient, treatment of critical ICP elevation (>20 mmHg) should proceed in the following steps: (1) consideration of repeat computed tomography (CT) scanning or consideration of definitive neurosurgical intervention, (2) intravenous sedation to attain a quiet, motionless state, (3) optimization of CPP to levels between 70 and 110 mmHg, (4) osmotherapy with mannitol or hypertonic saline, (5) hyperventilation (pCO2 26–30 mmHg), (6) high-dose pentobarbital therapy, and (7) systemic cooling to attain moderate hypothermia (32–33°C). Placement of an ICP monitor and use of a stepwise treatment algorithm are both essential for managing ICP effectively in the ICU setting.

Pathophysiology

Intracranial Compliance. The Monroe–Kellie doctrine dictates that the cranial vault is a fixed space that contains three compartments: blood, cerebrospinal fluid (CSF), and brain tissue. In the average adult, the brain volume is 1400 ml, the blood volume is 150 ml, and the CSF volume is 150 ml. CSF is produced by the choroid plexus in the ventricles at a rate of approximately 20 ml/hr, and drains into the venous system via the arachnoid villi and granulations [1]. This outflow is normally of low resistance; hence jugular venous pressure is the chief determinant of ICP in healthy patients. Normal ICP ranges from 50 to 200 mmH2O or 3–15 mmHg. In routine intensive care unit (ICU) practice, the goal of ICP management is to maintain levels below 20 mmHg.

In pathologic states characterized by increased ICP (Table 1), additional volume is added to the intracranial compartment. This can result from the addition of an extrinsic mass lesion or from an increase in the volume of CSF (hydrocephalus), brain tissue (cytotoxic edema), or blood (vasogenic edema). To maintain ICP within normal limits, these increases in intracranial volume are initially counterbalanced by volume reductions in the other compartments. CSF is displaced through the foramen magnum into the paraspinal space, blood is displaced from the intracranial to the extracranial venous system, and the brain parenchyma is compressed. After these mechanisms are exhausted,
intracranial compliance (ΔV/ΔP) falls sharply, and even small increases in intracranial volume can lead to dramatic elevations in ICP (Fig 1).

The relative state of intracranial compliance can be assessed by inspection of the ICP waveform (Fig 1, insets). ICP normally increases 2–3 mmHg with each arterial pulse because of transient increases in cerebral blood volume (CBV). When intracranial compliance is reduced, intracranial pulse pressure can reach levels of 10–15 mmHg, which reflects loss of the ability to accommodate even small pulsatile increases in CBV. As intracranial compliance falls, the morphology of the ICP waveform also changes, in that the amplitude of the second peak (the dicrotic wave) initially equals and then exceeds the amplitude of the first peak (the percussion wave) (Fig 2).

**Cerebral Perfusion Pressure.** Cerebral perfusion pressure (CPP), defined as the mean arterial pressure (MAP) minus ICP, is a critical determinant of cerebral blood flow (CBF) and plays an important role in ICP management. Normally CBF is “autoregulated” at a constant level over a wide range of CPPs (from 50 to 150 mmHg) (Fig 3). Pressure autoregulation of this type is mediated by changes in arteriolar diameter and cerebrovascular resistance. The autoregulatory curve is shifted to the left in children and shifted to the right in patients with chronic hypertension. In pathologic states with impaired autoregulation, such as TBI and subarachnoid hemorrhage, CBF may approximate a linear relationship with CPP, which creates a smaller range of optimal CPP (Fig 2). Reduction of CPP below the lower limit of autoregulation can lead to ischemia [2], whereas CPP elevation above the upper limit of autoregulation can be associated with hyperemia, exacerbation of vasogenic edema, and increased ICP [3]. Although the optimal CPP for any particular patient may vary, as a rule of thumb

**Table 1. Conditions Associated with Increased ICP**

<table>
<thead>
<tr>
<th>Intracranial mass lesions</th>
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<tr>
<td>Subdural hematoma</td>
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<tr>
<td>Epidural hematoma</td>
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<tr>
<td>Brain tumor</td>
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<tr>
<td>Cerebral abscess</td>
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<tr>
<td>Intracerebral hemorrhage</td>
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<tr>
<td>Increased brain volume (cytotoxic edema)</td>
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<tr>
<td>Cerebral infarction</td>
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<tr>
<td>Global hypoxia-ischemia</td>
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<tr>
<td>Reye’s syndrome</td>
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<tr>
<td>Acute hyponatremia</td>
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<tr>
<td>Increased blood and brain volume (vasogenic edema)</td>
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<tr>
<td>Hepatic encephalopathy</td>
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<tr>
<td>Traumatic brain injury</td>
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<tr>
<td>Meningitis</td>
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<tr>
<td>Encephalitis</td>
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<tr>
<td>Hypertensive encephalopathy</td>
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<tr>
<td>Eclampsia</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Dural sinus thrombosis</td>
</tr>
<tr>
<td>Altitude-related cerebral edema</td>
</tr>
<tr>
<td>Increased CSF volume</td>
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<tr>
<td>Communicating hydrocephalus</td>
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<tr>
<td>Noncommunicating hydrocephalus</td>
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<tr>
<td>Choroid plexus papilloma</td>
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![Fig 1. Intracranial pressure-volume relationship. At point A, on the flat portion of the curve, the amplitude of the arterial reflection in the ICP waveform is small (inset), and the addition of volume leads to a small increase, in pressure (A'). At point B, on a steeper portion of the curve, the intracranial compartment is relatively noncompliant, the amplitude of the arterial reflection in the ICP waveform is large (inset), and addition of the same amount of volume leads to a larger increase, in pressure (B'). (Reprinted from Mayer SA. Management of increased intracranial pressure. In: Wijdicks EFM, Diringer MN, Bolton CF, et al. Continuum: Critical Care. Minneapolis, MN: American Academy of Neurology, 1997:47–61.)](image1)

![Fig 2. ICP waveform in conditions of normal (top) and abnormal (bottom) intracranial compliance. (Reprinted from Chestnut RM, Marshall LF. Treatment of abnormal intracranial pressure. Neurosurg Clin N Am 1991;2:267–284.)](image2)
CPP should be maintained above 70 mmHg to avert ischemia, and below 110 mmHg to avoid breakthrough hyperperfusion. To accurately measure CPP in the ICU, the pressure transducer used to measure MAP must be set at head level [4].

CBF also depends upon PaCO₂ and PaO₂ levels. In general, the cerebral vessels are less responsive to changes in PaO₂ than to those in PaCO₂. Arteriolar diameter and CBF progressively increase as PaCO₂ rises from 20 to 80 mmHg, whereas hypoxemia leads to vasodilation and increased CBF only when PaO₂ falls below 50 mmHg [1].

**Pathologic ICP Waves.** Patients with reduced intracranial compliance and elevated ICP may develop pathologic ICP waves (Fig 4). Lundberg A waves (plateau waves) are dangerous elevations in ICP [5]. They occur suddenly, can reach levels of 50–100 mmHg, and can last from minutes to hours. Plateau waves are characteristically associated with “mirror” reductions in CPP (Fig 5). When severe, plateau waves are associated with reduced CPP and CBF, leading to global hypoxic-ischemic damage. Lundberg B waves are of lesser amplitude (5–20 mmHg) and of shorter duration (1–5 minutes) than A waves. Although they are not directly harmful, B waves are a useful marker of abnormal intracranial compliance. Both of these waves characteristically end with a surge in systemic blood pressure and ICP, known as a termination spike [5,6].

A vasodilatory cascade model has been proposed to explain the pathogenesis of pathologic ICP waves [6,7]. According to this model, pathologic A and B waves occur because CPP is inadequate. The process begins with a reduction in CPP, which results from a drop in MAP or a surge in ICP [6]. To maintain CBF, the cerebral vasculature dilates and CBV increases. This adds volume to the intracranial compartment, resulting in an increase in ICP and further reduction of CPP. This initiates a vicious cycle in which cerebral vasodilation continues until it is maximal, at which point a “plateau” is reached at a new level of increased CBV and ICP and decreased CPP and CBF. The plateau ends once CBF is inadequate to maintain tissue oxygenation and ischemia develops. This results in a reflex systemic pressor response mediated by a surge in systemic vascular resistance. MAP climbs and CPP is restored (the termination spike), which allows the...

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**Fig 3.** Cerebral autoregulation curve. In the normal relationship (solid line), with CBF held constant across a wide range of CPP (50–150 mmHg). In disease states (e.g., vasospasm, ischemia, intracranial mass lesion), cerebral blood flow may become pressure passive (dotted line). (Reprinted from Mayer SA. Management of increased intracranial pressure. In: Wijdicks EFM, Diringer MN, Bolton CF, et al. Continuum: Critical Care. Minneapolis, MN: American Academy of Neurology, 1997:47–61.)


**Fig 5.** Plateau waves followed by sustained ICP elevation in a patient with traumatic brain injury. Early in the course of the recording, plateau waves exceeding 90 mmHg are associated with “mirror” reductions in CPP below 50 mmHg. At the end of the recording, ICP remains elevated between 40 and 60 mmHg, MAP falls below 75 mmHg, and CPP drops to 20 mmHg. At this point the patient became clinically brain dead.
cerebral vessels to return to normal caliber, restoring CBV and ICP to normal levels.

Signs of Increased ICP and Herniation

The clinical manifestations of increased ICP are well known, but are notoriously unreliable (Table 2). A depressed level of consciousness and reflex hypertension, the two most consistent signs, both reflect the effects of globally reduced CBF. However, many patients have multiple reasons for a depressed level of consciousness, and in some patients with significant shift and mass effect, ICP may be normal. Comatose patients with intracerebral hemorrhage [8] and middle cerebral artery territory infarction [9], for instance, may have ICP levels that vary from normal to highly elevated, and brain stem herniation can occur in the absence of elevated ICP. Cushing’s triad (hypertension, bradycardia, and irregular respiration), which was originally described in response to elevated ICP, can also result from brain stem herniation. Because of the poor correlation between clinical signs and ICP, the only way to properly diagnose increased ICP is to directly measure it.

It is important to differentiate clinical signs of increased ICP from signs of cerebral herniation (Table 3). Brain tissue displacement and herniation occur when compartmentalized mass effect leads to ICP gradients [10,11]. Patients with intracranial mass lesions may have elevated ICP, brain tissue shifting, or both. Herniation is often rapidly fatal, but can be reversed by reducing mass effect related to compartmentalized ICP gradients with treatments such as mannitol, hypertonic saline, and hyperventilation.

ICP Monitoring

**Indications.** Invasive monitoring of ICP is generally indicated in patients who meet all three of the following criteria:

1. The patient is suspected to be at risk for elevated ICP.
2. The patient is comatose (Glasgow coma scale score ≤ 8).
3. The prognosis is such that aggressive ICU treatment is indicated.

Suspicion of increased ICP is usually based on clinical signs (Tables 2 and 3) and the results of a computed tomography (CT) scan showing significant intracranial mass effect with midline shift or effacement of the basal cisterns. However, in comatose patients with TBI, intracranial hypertension occurs in approximately 10% of patients with normal CT scans; this risk is even higher in patients more than 40 years old, with motor posturing, or with hypotension (systolic blood pressure < 90 mmHg) [12].

If a patient is awake and can follow commands, it is unlikely that ICP is dangerously elevated [13], and the benefits of ventricular drainage or ICP monitoring probably do not outweigh the risks. Careful monitoring of mental status in an ICU will usually suffice in these cases.

**Invasive ICP monitoring devices.** Empiric therapy for increased ICP (i.e., standing doses of mannitol) without invasive monitoring is a distressingly common practice. This approach is unsatisfactory.

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**Table 2. Clinical Signs of Increased ICP**

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<th>Signs which are almost always present</th>
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<tr>
<td>Depressed level of consciousness</td>
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<tr>
<td>(lethargy, stupor, coma)</td>
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<tr>
<td>Hypertension, with or without bradycardia</td>
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<table>
<thead>
<tr>
<th>Symptoms and signs which are sometimes present</th>
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<tbody>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Vomiting</td>
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<tr>
<td>Papilledema</td>
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<tr>
<td>Sixth cranial nerve palsy</td>
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**Table 3. Herniation Syndromes**

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical hallmark</th>
<th>Causes</th>
</tr>
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<tbody>
<tr>
<td>Uncal (lateral transtentorial)</td>
<td>Ipsilateral CN 3 palsy</td>
<td>Temporal lobe mass lesion</td>
</tr>
<tr>
<td></td>
<td>Contralateral motor posturing</td>
<td></td>
</tr>
<tr>
<td>Central transtentorial</td>
<td>Coma with progression from bilateral decortic to decerbrate posturing</td>
<td>Diffuse cerebral edema</td>
</tr>
<tr>
<td></td>
<td>Rostral-caudal loss of brain stem reflexes</td>
<td>Acute hydrocephalus</td>
</tr>
<tr>
<td>Subfalcine</td>
<td>Coma with asymmetric (contralateral &gt; ipsilateral) motor posturing</td>
<td>Convexity (frontal or parietal) mass lesion</td>
</tr>
<tr>
<td>Cerebellar</td>
<td>Sudden progression to coma with bilateral motor posturing in a patient with cerebellar signs</td>
<td>Cerebellar mass lesion</td>
</tr>
</tbody>
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because most ICP treatments are effective for a short time only, may lose their efficacy with prolonged use, and have side effects. Optimally therapy should be given when ICP is high, and withheld when it is normal. Only an invasive ICP monitor makes this possible. The four main types of invasive ICP monitors used in standard ICU practice are listed below, in general order of their accuracy and reliability (Fig 6).

INTRAVENTRICULAR CATHETERS. These devices directly connect the intracranial space to an external pressure transducer via saline-filled tubing. The bedside pressure transducer must be positioned at the level of the foramen of Monroe (external auditory meatus) to accurately reflect ICP. The catheter is usually connected to both a pressure transducer and an external drainage system via a three-way stopcock. The system can then be set for continuous ICP monitoring with intermittent CSF drainage or continuous drainage with intermittent ICP measurement. The major advantage to intraventricular catheters (IVCs) is that they allow treatment of increased ICP via drainage of CSF. The main disadvantage is the high risk of infection (ventriculitis or meningitis), which occurs in 10–20% of patients and increases dramatically after 5 days [14]. Most neurointensivists administer prophylactic antibiotics with gram-positive coverage, such as oxacillin 1–2 g every 6 hours, to minimize this risk. In a clinical trial of 228 IVC patients, prolonged therapy with ampicillin sulbactam in the ICU significantly reduced the frequency of CSF infection compared to patients given perioperative treatment only (3% versus 11%) [15].

INTRAPARENCHYMAL PRESSURE TRANSDUCERS. The pressure transducer in these disposable devices is incorporated into the tip of a thin fiberoptic cable (the Camino device) or within a strain-gauge microsensor at the tip of a flexible catheter (the Codman device). These catheters can be placed into either the brain parenchyma or the ventricle via a small burr hole and screw [16,17]. With intraparenchymal placement, the infection rate is exceedingly low (approximately 1%) [18]. When combined with a ventricular catheter, the system allows simultaneous CSF drainage and continuous ICP measurement. These devices only need to be calibrated once prior to insertion, and the accuracy of ICP measurements is generally superior to those provided by subarachnoid bolts or epidural transducers [19]. A new version of the Codman monitor also provides measurements of brain temperature. A third parenchymal monitor recently approved by U.S. Food and Drug Administration (FDA) (the Spielberg device) features a small air-filled balloon at the tip of a flexible catheter; it has the advantage of providing measurements of intracranial compliance (calculated as a pressure/volume index) as well as ICP [20].

SUBARACHNOID BOLTS. This is another fluid-coupled system which connects the intracranial space to an external transducer at the bedside via saline-filled tubing [21]. The subarachnoid bolt is actually a hollow screw that is inserted via a burr hole. The dura at the base of the bolt is perforated with a spinal needle, allowing the subarachnoid CSF to fill the bolt. Pressure tubing is then connected to establish communication with a pressure monitoring system. Although the infection risk is low, these devices are prone to error, including underestimation of ICP, screw displacement, and occlusion by debris [22].

EPIDURAL TRANSDUCERS. These devices (the Gaeltec device) are inserted deep into the inner table of the skull and superficial to the dura [23]. In most of these devices, pressure is transduced by an optical sensor. They have a low infection rate (approximately 1%) [17], but are prone to malfunction, displacement, and baseline drift that can exceed 5–10 mmHg after more than a few days of use. Much of the inaccuracy results from having the relatively inelastic dura between the sensor tip and the subarachnoid space.

Noninvasive ICP Monitoring. At present there is no noninvasive method that can provide accurate continuous on-line measurement of ICP. However, transcranial Doppler (TCD) ultrasonography, which measures the velocity of blood flow in the
basal cerebral arteries, shows characteristic changes with increasing ICP [24]. As CPP falls, diastolic velocity decreases and pulsatility increases, reflecting increased distal vascular resistance to flow. Though this finding is specific for severe intracranial hypertension, TCD is not sensitive to mild to moderate ICP elevations. Lateralized asymmetries in TCD pulsatility correlate with lesion volume in intracerebral hemorrhage, and are believed to reflect compartmentalized ICP gradients [25]. Promising new applications using ultrasound technology to estimate ICP noninvasively have been described, but have not yet been validated in the clinical setting [26–28].

**Adjuncts to ICP Monitoring.** Several new modalities have recently been introduced that can provide additional information regarding the adequacy of cerebral perfusion and the extent of injury in patients undergoing ICP monitoring.

**JUGULAR VENOUS OXYGEN SATURATION (SJvO2) AND BRAIN TISSUE PO2 (PbtO2) MONITORING.** SJvO2 monitoring assesses the adequacy of global cerebral oxygen delivery, whereas PbtO2 monitoring measures regional oxygen tension. Both emerging technologies provide continuous information regarding the adequacy of CPP and CBF at the tissue level [29–31]. SJvO2 is measured with a 5-French fiberoptic oxygen saturation catheter placed retrograde in the internal jugular vein so that the tip is positioned in the jugular bulb; PbtO2 is measured with a miniaturized Clark electrode embedded in the tip of a thin catheter inserted 3–4 cm into the cerebral white matter (the Licox or Neurotrend device). Both techniques can detect inadequate CBF (i.e., ischemia), which may occur even in patients with relatively normal CPP [32], and excessive CBF (i.e., hyperemia), which can aggrivate ICP related to vasogenic edema and breakthrough of autoregulation [33]. Accordingly these monitors can be used to optimize therapy; mannitol and vasopressor infusion reduce ICP and improve cerebral oxygenation when SJvO2 or PbtO2 values fall below critical levels [30–32], whereas hyperventilation reduces ICP and tissue oxygenation when it is supranormal due to relative hyperperfusion [31] (Table 4). The depth and duration of ischemia detected by either device is highly correlated with poor clinical outcome in patients with severe TBI [30,31]. Since neither monitor alone can detect all episodes of ischemia [34], selection of which type to use depends on the specific clinical circumstances at hand. PbtO2 monitoring is generally easier to use, and is most desirable when detection of ischemia in a specific brain region is the predominant concern, whereas SJvO2 is less influenced by high FiO2 levels and hence may be a more reliable measure of relative hyperperfusion [34].

**CEREBRAL MICRODIALYSIS.** This adjunctive monitoring technique is labor intensive and has yet to gain widespread acceptance. A probe is placed through the skull and levels of different substances may be measured using high-performance liquid chromatography (HPLC). Lactate, glutamate, and more recently extracellular potassium have been measured using this microdialysis. These levels correlate with cerebral ischemia and poor outcome [35].

**MULTIMODAL MONITORING.** Finally, a combination of multiple monitoring techniques may soon be possible. Various prototypes are in development that can allow simultaneous monitoring of ICP, PbtO2, PbtCO2, pH, brain temperature, laser Doppler flow, and even microdialysis.

### Management of Increased ICP

**General Care Issues.** Proper management of all critically ill brain-injured patients begins with general care issues designed to optimize oxygenation and cerebral blood flow and to minimize factors that can aggravate neuronal injury or trigger ICP elevations. The following guidelines should be followed in all patients at risk for increased ICP:

**PATIENT POSITIONING.** As long as the patient is not hypotensive (mean blood pressure < 60 mmHg), the head of the bed should be elevated to 30 degrees and a straight head position should be maintained. Head elevation to 30 degrees reduces ICP by reducing jugular and cerebral venous pressure and enhancing venous outflow, without significantly lowering CPP, CBF, or cardiac output [36,37]. Some have recommended a head flat position to prevent any reductions of CPP that

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**Table 4. Normal and Critical Values for SJvO2 and PbtO2 Monitors**

<table>
<thead>
<tr>
<th>SJvO2 (%)</th>
<th>PbtO2 (mm Hg)</th>
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<tbody>
<tr>
<td>Normal valuea</td>
<td>62</td>
</tr>
<tr>
<td>Critical upper limit (indicates hyperemia)</td>
<td>80</td>
</tr>
<tr>
<td>Critical lower limit (indicates ischemia)</td>
<td>50</td>
</tr>
<tr>
<td>Average value in severe TBIa</td>
<td>73 ± 10</td>
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NA = data not available. Interpretation of critical values assumes normal FiO2 (<40%) and hematocrit. aData from reference 34.
may occur with head elevation, which may be reasonable in selected cases [38]. However, head elevation in excess of 45 degrees should generally be avoided because paradoxical increases in ICP can occur in response to excessive CPP reduction [39]. Sharp head angulation should also be avoided, as it may cause jugular venous compression, increased venous backpressure, and increased ICP.

FLUID MANAGEMENT. Only isotonic fluids, such as 0.9% (normal) saline or lactated Ringer’s solution, should be used in patients at risk for elevated ICP. Cerebral edema is generally understood to result from the creation of “idiogenic osmoles” which draw water down an osmolar gradient into injured brain tissue. Hypotonic fluids such as 5% dextrose or 0.45% (half-normal) saline should be strictly avoided because the free water contained in these fluids can aggravate cerebral edema and increase ICP [40]. Systemic hypo-osmolality (<280 mOsm/L) should be aggressively treated with mannitol or 3% hypertonic saline. The traditional practice of restricting total fluid intake (dehydration therapy), with the goal of reducing the extracellular fluid volume, has not been shown to significantly impact brain water content or ICP. In fact, hypovolemia may lead to inadequate CPP and a consequent increase in ICP [41].

Patients with elevated ICP should have a central venous line placed to monitor central venous pressure; this is particularly critical for patients treated with mannitol or hypertonic saline. As a general rule, a central venous pressure greater than 5 mmHg and equal to slightly positive daily net fluid balance should be maintained by increasing the rate of infusion of isotonic crystalloid, administering 0.9% saline or 5% albumin fluid boluses, or transfusing blood to maintain hematocrit at greater than 24% [42].

Use of 1.5–3% hypertonic saline as a maintenance intravenous fluid for patients with cerebral edema is gaining popularity in the neurocritical care community. Though support for this practice to date is inconclusive, adequate clinical trials have yet to be performed [43]. A small study of pediatric TBI patients compared the use of 1.6% saline with lactated Ringer’s solution and found no differences in ICP or CPP, though the hypertonic saline group required fewer interventions to lower ICP [44]. Lack of uniform concentrations and poor definition of dose-response relationships has limited the widespread use of hypertonic saline to date.

TEMPERATURE MANAGEMENT. Fevers should be treated aggressively. Temperature elevations increase ICP by increasing cerebral metabolism and blood flow, and have been shown to exacerbate hypoxic-ischemic neuronal injury in experimental animals [45]. As a general standard, acetaminophen and cooling blankets should be given to all patients with sustained fevers in excess of 38.3°C (101.0°F), but evidence for their efficacy in neurologic patients is scant [46,47]. Endovascular cooling with the use of closed-circuit water-circulating intravenous catheters is a promising new approach that is currently under development.

Recent studies suggest that indomethacin may be the ideal antipyretic to use in patients with increased ICP. Indomethacin has been shown to decrease CBF and ICP in animal models and patients with TBI [48]. The mechanism of action is not known, but may involve vasoconstriction of cerebral vessels and inhibition of prostaglandin synthesis [48].

SEIZURE PROPHYLAXIS. Seizures can lead to profound elevations of CBF, CBV, and ICP, even in patients who are sedated or paralyzed [49]. This is secondary to the increased cerebral metabolic demand that occurs with seizures. Intravenous fosphenytoin (15–20 mg/kg loading dose, 3–5 mg/kg/day) is the preferred agent for seizure prophylaxis while in the ICU.

STEROIDS. Dexamethasone and other steroids should not be used as a standard treatment for ICP because they are ineffective against cytotoxic edema [50]. There is generally no role for steroids in the treatment of mass effect related to cerebral infarction [51], intracerebral hemorrhage [52], or TBI [53]. By contrast, vasogenic edema related to neoplasm or abscess is steroid responsive, and dexamethasone 4–20 mg every 6 hours can lead to dramatic reductions in lesion volume [54].

Emergent Treatment of Increased ICP in an Unmonitored Patient. Emergency measures for ICP control (Table 5) are appropriate for comatose patients who present acutely with clinical signs of increased ICP or herniation. These measures are

<table>
<thead>
<tr>
<th>Table 5. Emergency Measures for ICP Reduction</th>
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<tr>
<td>1. Elevate head of bed 15–30 degrees.</td>
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<td>2. Normal saline (0.9%) at 80–100 cc/hr</td>
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<td>(avoid hypotonic fluids).</td>
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<tr>
<td>3. Intubate and hyperventilate (target pCO2</td>
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<td>26–30 mmHg).</td>
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<td>4. Mannitol 20% 1–1.5 g/kg via rapid intravenous infusion.</td>
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<tr>
<td>5. Foley catheter.</td>
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<tr>
<td>6. CT scan and urgent neurosurgical</td>
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<td>consultation.</td>
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designed to lower ICP as quickly and effectively as possible in order to “buy time” before a definitive neurosurgical procedure (craniotomy, ventriculostomy, or placement of an ICP monitor) can be performed. Aggressive hyperventilation and mannitol therapy are the cornerstones of this type of intervention.

Stepwise Treatment Protocol for Elevated ICP in a Monitored Patient. The primary goal of ICP management in a monitored patient is to maintain ICP below 20 mmHg and CPP above 70 mmHg. Contemporary ICP management has changed in recent years in two important aspects: CPP management (in addition to ICP control) has become increasingly emphasized, and the potential for overzealous hyperventilation to cause excessive vasoconstriction and aggravate ischemia has become increasingly recognized. The stepwise protocol presented here for managing ICP in a monitored patient (Table 6) reflects these considerations. More than one step may be instituted simultaneously, but only after all of the preceding steps have been addressed. Likewise, ICP therapy should be withdrawn in a similar stepwise fashion (Fig 7). This algorithm should be initiated any time ICP remains greater than 20 mmHg for more than 10 minutes.

Though we favor the protocol presented below because of its simplicity, other treatment algorithms may be equally effective. Use of a standardized, evidence-based protocol for ICP management allows for efficient and well-coordinated treatment of patients within an institution, and can improve patient outcomes. In a retrospective study of patients with TBI, patients treated with a standardized algorithm of instituting and weaning ICP therapies required fewer interventions and had a shorter duration of treatment than patients treated ad hoc [55].

Table 6. Stepwise Treatment Protocol for Elevated ICP* in a Monitored Patient

1. Surgical decompression. Consider repeat CT scanning and definitive surgical intervention or ventricular drainage.
2. Sedation. Intravenous sedation to attain a motionless, quiet state.
3. CPP optimization. Pressor infusion if CPP is less than 70 mmHg, or reduction of blood pressure if CPP is greater than 110 mmHg.
4. Osmotherapy. Mannitol 0.25–1.0 g/kg intravenously (repeat every 1–6 hours as needed).
5. Hyperventilation. Target pCO2 levels of 26–30 mmHg.
6. High-dose pentobarbital therapy. Load with 5–20 mg/kg, infuse 1–4 mg/kg/hr.
7. Hypothermia. Cool core body temperature to 32–33°C.

*More than 20 mmHg for more than 10 minutes. Refer to text for details.

Fig. 7. The Columbia stepwise protocol for ICP management.

STEP 1: SURGICAL DECOMPRESSION OR CSF DRAINAGE. The first consideration in the face of an acute increase in ICP should always be whether a definitive intervention, such as craniotomy or ventriculostomy, should be performed to remove volume or decompress the skull. A repeat CT scan should be considered to rule out reaccumulation of an intracranial hemorrhage or worsening hydrocephalus. If a ventricular catheter is in place, the system should be opened to drainage and 5–10 ml of CSF removed.

The option of some definitive surgical intervention should be continuously evaluated as additional steps to control ICP are added. Controlled lumbar CSF drainage (5–20 ml/hr) has been reported to reduce ICP and increase CPP in patients refractory to medical therapy and ventricular drainage alone [56]. However, this intervention is feasible only if the basal cisterns are open on CT, and even in these cases, transtentorial herniation remains a risk. Decompressive hemicraniectomy is becoming increasingly used as an intervention of last resort for patients who might otherwise require pentobarbital or hypothermia. Wide cranial decompression can definitively control ICP and reverse brain stem herniation, and has been reported to be effective for treating massive cerebral infarction [57], encephalitis [58], head trauma [59], and intracerebral hemorrhage [60] in nonrandomized studies. Complications of hemicraniectomy can include CSF leakage, local wound infection or meningitis, intracranial bleeding, and late hydrocephalus.

STEP 2: SEDATION. Sedation is often overlooked as a key factor in ICP control. In patients with reduced intracranial compliance, fighting against physical restraints or “bucking” the ventilator can increase
ICP by elevating intrathoracic and jugular venous pressure. Arterial hypertension associated with agitation may further increase ICP if the patient is at the upper range of the autoregulatory curve. Before further measures are instituted, agitated patients with increased ICP should be sedated to the point where they are quiet and motionless (Ramsey level 5 or 6). A combination of a sedative-hypnotic and analgesic agent is usually most effective (Table 7). The preferred regimen is the combination of an opioid, such as fentanyl (1–3 μg/kg/hr) or sufentanil (0.1–0.6 μg/kg/hr), to provide analgesia and propofol (0.3–3 mg/kg/hr) for sedation. It is important to use drugs that are short acting, such that the agent may be stopped for frequent neurologic assessments throughout the day. One study showed that daily, scheduled interruption of sedation to examine patients not only reduced the length of ventilator dependence and ICU length of stay, but also decreased the need for other tests such as brain imaging and lumbar punctures to evaluate alterations in mental status [61].

Neurocritical care patients, even when comatose, can sense pain and require analgesia in addition to sedation. Therefore careful use of a low-dose continuous infusion opioid in addition to propofol or midazolam is recommended. Bolus injections of opioids, however, should be used with caution in patients with elevated ICP. Bolus infusions of the sufentanil, fentanyl, and alfentanil can transiently lower MAP and increase ICP due to autoregulatory vasodilation of cerebral vessels [62]. This effect is seen primarily in patients with intact autoregulation, but can also occur in patients with abnormal autoregulation [63]. Vaspressors may be used to avoid hypotension and possible reflex ICP elevation.

Propofol may be the ideal sedative to use in patients with elevated ICP; besides the fact that it is ultrashort acting, it has favorable effects on ICP and seizure activity, and may have neuroprotective properties. In a study comparing propofol to morphine in patients with severe TBI, patients treated with propofol had lower ICP values and more favorable long-term neurologic outcomes [64]. By contrast, paralysis with neuromuscular blocking agents such as vecuronium, pancuronium, or cis-atracurium is rarely necessary, and places patients at risk for prolonged paralysis due to critical illness myopathy.

STEP 3: CPP OPTIMIZATION. If CPP is less than 70 mmHg and ICP is greater than 20 mmHg, elevation of mean arterial blood pressure and CPP with a vasopressor such as dopamine or phenylephrine (Table 8) can lead to a reflex reduction of ICP, by eliminating cerebral vasodilation that occurs in response to inadequate perfusion (Fig 8). CPP optimization to levels well above 70 mmHg may be desirable in chronically hypertensive patients (whose autoregulatory curve is shifted to the right), or in patients with low PbO₂ or SjvO₂ levels or Lundberg A and B waves (since these findings generally reflect insufficient CPP). The widely accepted “one size fits all” approach to CPP management (>70 mmHg) is in all likelihood an oversimplification, and efforts should be made to optimize CPP whenever patients fail standard therapy. One study that attempted to define optimal CPP levels for severe TBI patients by analyzing receiver-operating curves found that a CPP of 55 mmHg was the critical threshold for poor outcome in adults [65]. It seems prudent to maintain CPP well above this level in clinical practice, however, to provide an extra margin of safety. In an uncontrolled study of TBI patients with CPP maintained above 70 mmHg with phenylephrine and

### Table 7. Selected Short-Acting Intravenous Sedatives for ICP Management

<table>
<thead>
<tr>
<th>Agent</th>
<th>Pharmacology</th>
<th>Dosage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine sulfate</td>
<td>Opioid (sedative-hypnotic with analgesic properties)</td>
<td>2–5 mg IVP every 1–4 hours</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Opioid (short acting, 100 times more potent than morphine)</td>
<td>0.5–3.0 μg/kg/hr</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>Opioid (ultrashort acting)</td>
<td>0.1–0.6 μg/kg/hr</td>
</tr>
<tr>
<td>Propofol</td>
<td>Alkylphenol (ultrashort acting)</td>
<td>0.6–6 mg/kg/hr</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Benzodiazonepine (short acting)</td>
<td>0.05–0.1 mg/kg/hr</td>
</tr>
</tbody>
</table>

Dosages are approximate and should be titrated to the patient’s level of agitation and ICP. A combination of a sedative-analgesic and sedative-hypnotic agent may be more effective than the use of a single agent.
norepinephrine, better outcomes were obtained than in previously reported patients with strictly ICP-based management [41].

If MAP and ICP are elevated in a sedated patient, treatment of arterial hypertension can sometimes lead to a parallel reduction of ICP. If CPP is greater than 110 mmHg and ICP is greater than 20 mmHg, hypertension should be carefully treated with a short-acting agent (Table 7). However, extreme caution should be used to avoid reduction of CPP below 70 mmHg, which can trigger reflex cerebral vasodilation and ICP elevation. Nitroprusside can be particularly troublesome in this regard, and concerns also exist regarding the potential for nitroprusside to directly dilate the cerebral vasculature and increase ICP. For these reasons, nitroprusside is best avoided in patients with elevated ICP, and should only be used if an ICP monitor is in place. Experimental and clinical studies have demonstrated that treatment of hypertension in patients with intracerebral hemorrhage does not exacerbate perilesional ischemia [66] or cause reflex vasodilation and increased ICP [67], as long as CPP remains within the normal range.

**STEP 4: OSMOTHERAPY.** If CPP is optimized, the patient is sedated, and ICP remains elevated, mannitol or hypertonic saline should be given. Mannitol, an osmotic diuretic, lowers ICP via its cerebral dehydrating effects. The effects of mannitol are biphasic. Rapid infusion immediately creates an osmotic gradient across the blood-brain barrier, which leads to movement of water from brain parenchyma to the intravascular compartment. The result is decreased brain tissue volume, and hence reduced ICP [68]. The secondary effect of mannitol results from its action as an osmotic diuretic. As mannitol is cleared by the kidneys, it leads to free water clearance and increased serum osmolality. This leads to a more prolonged intracellular dehydrating effect as water flows down the osmotic gradient from the intracellular to the extracellular space.

The initial dose of mannitol 20% solution is 1–1.5 g/kg, followed every 1–6 hours with doses of 0.25–1 g/kg as needed. Repeated mannitol doses should be given on the basis of ICP measurements rather than as scheduled doses, unless the goal is to establish and maintain a hyperosmolar state (300–320 mOsm/L). The effect of a mannitol bolus on ICP begins within 10–20 minutes, reaches its peak between 20 and 60 minutes, and lasts for 4–6 hours, but this may vary widely between patients. Adverse effects of mannitol therapy include exacerbation of congestive heart failure (due to the initial intravascular volume expansion); volume contraction, hypokalemia, and profound hyperosmolality (after prolonged use); acute tubular necrosis (due to excessive hyperosmolality); and “rebound” increases in ICP [69]. Patients treated repeatedly with mannitol require frequent measurements of serum electrolytes and osmolality, careful recording of fluid input and output, and central venous pressure monitoring. Urinary volume losses should be replaced with normal (0.9%) saline to avoid volume depletion.

Bolus infusion of 3%, 7.5%, 10%, or 24.3% hypertonic saline is gaining popularity as an alternative to bolus infusions of mannitol for ICP crises [43]. In an uncontrolled study of 3% saline/
acetate infusion (75–150 ml/hr) and intermittent boluses (250 ml) titrated to maintain serum sodium levels between 145 and 155 mEq/L, hypertonic saline lowered ICP related to TBI and brain tumors, but not in patients with intracerebral hemorrhage or cerebral infarction [70]. Infusion of 2–5 ml/kg of 7.5% saline or 0.5–1.0 ml/kg of 23.4% saline over 30 minutes has also been shown to lower elevated ICP and augment CPP, with an effect that lasts several hours [71,72]. A large head-to-head trial of mannitol versus hypertonic saline is warranted.

STEP 5: HYPERVENTILATION. As a general rule, the goal of hyperventilation for ICP control should be to lower pCO₂ to 30 mmHg, or to 25–30 mmHg in extreme cases. The respiratory alkalosis caused by hyperventilation lowers ICP by causing cerebral vasoconstriction and reduced CBV [1]. The peak effect of hyperventilation on ICP is generally reached within 30 minutes. Over the next 1–3 hours the effect gradually diminishes, as compensatory acid-base buffering mechanisms correct the alkalosis within the central nervous system [1]. In patients with elevated ICP due to hyperemia and increased CBV, however, the effect may be prolonged, and hyperventilation may be the treatment of choice [73]. Hyperventilation should be tapered slowly over 4–6 hours because abrupt cessation may lead to vasodilation and rebound increases in ICP.

Though it is postulated that prolonged severe hyperventilation (pCO₂ < 25 mmHg) can actually exacerbate cerebral ischemia by causing profound vasoconstriction, the deleterious effects of excessive hyperventilation may also include more labile ICP. In a study of patients with TBI, prophylactic hyperventilation to a pCO₂ of 25 mmHg resulted in poorer outcome compared with normally ventilated patients [74]. The authors hypothesized that blood vessels may become hypersensitive to changes in pCO₂ after prolonged hyperventilation because CSF buffering capacity is lost. In cases of pediatric head trauma, profound hypocarbia was associated with decreased cerebral oxygen consumption and ischemia [75]. SjvO₂ monitoring is a useful modality for ensuring that prolonged aggressive hyperventilation, if necessary, is not critically reducing oxygen delivery to the brain.

STEP 6: PENTOBARBITAL THERAPY. High-dose barbiturate therapy, given in doses equivalent general anesthesia, can effectively lower ICP in most patients refractory to the steps outlined above [76,77]. The effect of pentobarbital is multifactorial, but most likely stems from a profound reduction of cerebral metabolism, which is coupled to reductions of CBF and CBV [78]. Pentobarbital often causes hypotension, and usually requires the use of vasopressors to maintain CPP above 70 mmHg.

Pentobarbital typically requires a loading dose of 10–20 mg/kg, given in repeated 5 mg/kg boluses, until a state of flaccid coma with preserved pupillary reactivity is attained. Maintenance infusion is usually about 1–4 mg/kg/hr. Continuous EEG monitoring is helpful to avoid oversedation, since generally no further ICP reduction occurs once a burst-suppression pattern is attained. If ICP is normalized with pentobarbital, it is generally maintained for 24–48 hours. It can then be abruptly discontinued because its highly lipophilic nature and long halftime (90 hours) result in a gradual reduction of blood levels over several days.

STEP 7: HYPOTHERMIA. Systemic hypothermia to levels of 32–33°C can lower ICP in some patients refractory to pentobarbital [79–81]. This technique requires placement of cooling blankets under and over the patient, iced gastric lavage, and pharmacologic paralysis with vecuronium or a similar neuromuscular blocking agent to prevent shivering. Prolonged hypothermia can be dangerous because of increased risk of infectious complications, coagulopathy, and electrolyte derangements, among other hazards. Rewarming should always be done slowly, over at least a day, and passively, without active heating, to avoid rebound cerebral edema or a systemic inflammatory response syndrome, which can be fatal.

In a small randomized controlled trial of severe TBI patients refractory to pentobarbital, mild-to-moderate hypothermia (34°C) significantly reduced ICP, improved CPP, reduced CBF and cerebral metabolic rate (CMRO₂), and reduced arteriovenous venous oxygen differences [79]. Survival was 50% in hypothermia patients compared to 18% in the control group (p < 0.05). Later studies by the same group reported that hypothermia was most effective for pentobarbital-refractory ICP elevations between 20 and 40 mmHg [80], and that severe TBI patients with low ICP do not benefit from hypothermia [81]. These reports, and the negative results of a recent large National Institutes of Health (NIH)-funded trial studying the effects of hypothermia as first-line therapy for severe TBI [82], suggest that hypothermia is not effective as a primary form of neuroprotection for severe TBI related to diffuse axonal injury.

References