

Review Article

Intracranial Hypertension:
Therapeutic and Anesthetic Considerations

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Since the last review of neuroanesthesia in this journal, written six years ago by Michenfelder and associates, new concepts and techniques in the management of patients with elevated intracranial pressure (ICP) have emerged. These advances have largely emanated from laboratories and clinics involved in measurement of ICP, cerebral blood flow (CBF), and cerebral metabolism.

This new information is reviewed in the context of our present knowledge of the physiologic and pharmacologic factors influencing CBF and ICP. A protocol for pre- and postoperative evaluation of neurologic function in patients with intracranial disease is presented, and specialized monitoring techniques for neurologic intensive care are reviewed. ICP changes associated with specific intracranial lesions are considered, together with the indications for and effects of therapy directed toward reduction of intracranial hypertension.

Pathophysiology of Intracranial Hypertension

INTRACRANIAL COMPLIANCE AND INTRACRANIAL PRESSURE

Understanding normal CSF circulatory dynamics is a prerequisite to management of

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<th>ABBREVIATIONS</th>
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<tr>
<td>BBB = blood-brain barrier</td>
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<tr>
<td>BP = arterial blood pressure</td>
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<td>CBF = cerebral blood flow</td>
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<td>CSF = cerebrospinal fluid</td>
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<td>CBV = cerebral blood volume</td>
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<tr>
<td>CPP = cerebral perfusion pressure</td>
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<td>ICP = intracranial pressure</td>
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pathologic elevations in ICP. Figure 1 shows the cerebral vasculature and cerebrospinal fluid (CSF) circulatory pathways as they are situated within the semiclosed rigid containment of the skull. In this situation a change in the volume of any intracranial component (blood, CSF or brain) must be reflected by a reciprocal change in one or both of the other elements if pressure change is to be avoided.58

For instance, initially a slow increase in brain volume due to tumor and/or edema will displace some CSF from within the head through the foramen magnum into the distensible spinal subarachnoid space (represented by the bellows in fig. 1). As ICP begins to rise, CSF absorption, which is to some extent pressure-dependent,57 can increase, providing some additional ICP buffering. With time, the overall CSF content in the cerebrospinal axis is reduced. When this major volume-buffering mechanism is exhausted, further spatial compensation can be achieved by reduction in intracranial cerebral blood volume (CBV) by compression of the low-pressure venous system.

Progressive enlargement of an intracranial mass eventually leads to distortion and blockage of the subarachnoid pathways. This exhausts CSF translocation as the major means of ICP buffering for expanding intracranial lesions. An example of this situation is represented in figure 2. Here, brain enlargement has lead to encroachment of the foramen magnum, collapse of the large CSF cistern, and compression of the arachnoid villi. Depending upon intraparenchymal pressure gradients and mechanical tissue compression, localized vasodilation and vasoconstriction or vascular collapse may coexist. Collapse of the bridging veins entering the sagittal sinus or of the extracranial jugular venous outflow tract.
can further complicate the situation by creating a back-pressure, which is transmitted into the brain's capillary bed. In a compensatory effort to maintain CBF during intracranial hypertension, a reduction in upstream arterial resistance may occur.\textsuperscript{49} This leads to further regional or total CBV augmentation if arterial hypertension supervenes. These arterial and venous vascular resistance and pressure changes lead to elevated capillary pressure and predispose to the formation of cerebral edema.\textsuperscript{84} When progressive edema and/or tumor growth has been maximally accommodated by intracranial CSF and blood volume reduction, the enlarged brain herniates through the tentorial notch or into the foramen magnum, as shown in figure 2.

Intracranial volume-pressure relationships can be described by a compliance curve like that shown in figure 3.\textsuperscript{58,83} During initial spatial compensation (between points 1 and 2), little ICP increase occurs. At point 2 compliance is reduced and further volume additions elicit progressive ICP elevation. When ICP is already high (point 3), even small increases in the intracranial volume will result in marked intracranial hypertension (between points 3 and 4), and anesthetic agents and techniques altering cerebral blood volume will markedly change ICP. The shape of the compliance curve in individual patients is highly variable and is determined by the interaction of lesion mass and location, and the presence of cerebral tissue herniation, as well as by blood pressure and $P_{\text{aCO}_2}$.\textsuperscript{63}

Figure 3 indicates that measurement of the ICP alone when it is within the normal range (10–15 torr supine), between points 1 and 2, may have little predictive value regarding a subsequent ICP elevation. In this situation intracranial compliance can be determined by the rapid injection or withdrawal of small volumes (0.1–1.0 ml) of sterile saline solution (without the preservative additive) or CSF through a lateral ventricular cannula, noting the resulting ICP change.\textsuperscript{63,83} This test should be applied cautiously. A strictly qualitative measure of compliance can be obtained by successive application of unilateral and bilateral manual compression of the internal jugular veins. This provides a rapidly reversible unquantified volume challenge to the intracranial space, and in our institution this technique is used to establish continued patency of the CSF ventricular recording catheter, as well as for qualitatively determining intracranial compliance. When CBF is high, jugular compression probably produces a greater CBV increase than the volume challenge given during a formal compliance test.

![Diagram](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931526/)

**FIG. 4.** Cerebral blood flow changes due to alterations in $P_{\text{aCO}_2}$ (—–), $P_{\text{aO}_2}$ (●●●) and blood pressure (—). The other two variables remain stable at normal values when the remaining variable is altered.

![Diagram](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931526/)

**FIG. 3.** Idealized intracranial volume–pressure relationships. See text.

**CEREBRAL BLOOD FLOW AND INTRACRANIAL PRESSURE**

Normally, CBF depends on arterial blood pressure (BP), $P_{\text{aCO}_2}$, and $P_{\text{aO}_2}$.\textsuperscript{98,129} These relationships are graphically summarized in figure 4. CBF varies directly with $P_{\text{aCO}_2}$ and inversely with $P_{\text{aO}_2}$. Cerebral flow is most sensitive to CO\textsubscript{2} within physiologic ranges of carbon dioxide tension. Conversely, oxygen
exerts its greatest influence over CBF when $\text{P}_{\text{a}}\text{O}_2$ falls below normal limits. Between approximate mean BP’s of 50 and 150 torr, CBF remains constant provided that arterial pressure changes relatively slowly. This phenomenon is called “autoregulation.”

In patients with hypertensive disease both the upper and the lower limits of autoregulation are shifted upwards.\textsuperscript{90,122} For instance, in awake hypertensive patients with mean BP’s between 125 and 180 torr the lower limits of autoregulation ranged from 90 to 125 torr.\textsuperscript{133} However, clinical signs of cerebral hypoxia in these patients did not occur until the mean BP was in the 35–80-torr range. Abrupt and large increases in BP cause a breakthrough of the upper limit of autoregulation wherein CBF increases in focal areas of the brain are accompanied by plasma protein penetration into the brain.\textsuperscript{46,47,132} This is probably due to overdistention of the capillaries, which leads to breakdown of the blood–brain barrier with cerebral edema formation and may play a role in hypertensive encephalopathy.\textsuperscript{46,120}

Maintenance of normal CBF during BP fluctuations implies changes in cerebrovascular resistance that relate inversely to the diameter of the cerebral resistance vessels. When autoregulation is intact CBV actually decreases by 0.015 ml/100 g/torr over a BP range of 35–200 torr.\textsuperscript{38} This is diagrammatically indicated in figure 5 (left). Cerebral acidosis, such as that caused by hypercapnia or acid accumulation in ischemic brain tissue (in toto or in local areas), can abolish or modify autoregulation, as noted in figure 5 (right).\textsuperscript{5,24}

Increases in CBF normally require reduced cerebrovascular resistance, and this implies a more dilated cerebrovascular tree. Augmentation of intracranial blood volume, therefore, can occur when CBF is increased. In normal brain, over a $\text{P}_{\text{a}}\text{CO}_2$ range of approximately 20–80 torr, CBF changes about 2 ml/100 g/torr change in $\text{CO}_2$ and CBV about 0.04 ml/100 g/torr change in $\text{CO}_2$.\textsuperscript{33} In a normal brain weighing 1,400 g this amounts to a 33-ml change in total CBV. CBF changes usually do not result in significant ICP elevation, because intracranial compliance is high. When compliance is reduced the CBF ordinate in figures 4 and 5 can be interpreted as qualitatively indicating the directional change in ICP. For instance, $\text{CO}_2$ retention elevates ICP in patients who have brain tumors.

**Progressive Intracranial Hypertension**

Progressive elevation of ICP eventually leads to a local or generalized reduction in cerebral perfusion pressure (CPP).\textsuperscript{118} Reduction of CPP to below the autoregulatory level causes ischemia, and acidic metabolites accumulate in the tissue, inciting a fixed reduction in cerebrovascular tone (called “cerebrovasomotor paralysis”).\textsuperscript{3,59,60} In this situation the ICP and CBF progressively become more passively related to BP. Small declines in BP can now cause regional or total cerebral ischemia, whereas marked elevations in BP not only increase CBF, but also initiate increases in CBV, enhance cerebral
edema formation, and elevate ICP.\textsuperscript{112,117} Therefore, an initially increased CBF due to BP elevation may lead to a progressively decreasing CPP. Cerebral ischemia may then occur when the BP strays above or below some critical set point. In individual cases the optimal BP can be determined only by measurement of ICP and CBF. The clinical message: avoid inducing extreme BP fluctuations. The pathologic cycle established by the above sequence is indicated in figure 6.

Anesthesics and Intracranial Pressure

Volatile Anesthetics, Autoregulation, and ICP

Anesthetic drugs alter ICP according to their abilities to increase or decrease cerebrovascular volume. These volume changes may be severe enough to cause herniation of cerebral tissue.\textsuperscript{27}

Anesthetics with cerebral vasodilatory actions could also potentiate the formation of cerebral edema, especially if blood pressure remains high.\textsuperscript{47,54} Administration of papaverine or carbon dioxide to animals subsequently subjected to acute arterial hypertension greatly enhanced transudation of protein-bound Evans blue dye.\textsuperscript{23,47} In effect, these vasodilating agents potentiate upper-limit autoregulatory breakthrough to increased arterial pressure, as discussed in the previous section. Studies documenting this phenomenon with regard to breakdown of the blood–brain barrier caused by anesthetics have not been reported.

Evaluation of anesthetic agents for neurosurgical patients requires consideration not only of their ICP effects but also of their potential to reduce blood pressure and cause focal or generalized cerebral ischemia, with or without a concomitant increase in ICP. When intracranial hypertension exists it is not sufficient to calculate the cerebral perfusion pressure (CPP) from the BP minus the jugular venous pressure. The jugular venous system is extracranial and represents systemic venous pressure. As ICP increases, CPP = BP – ICP. Therefore, measurement of BP alone in patients with intracranial hypertention cannot provide adequate warning of impending or actual critical reductions in CPP. Autoregulation in response to increase ICP appears to remain intact so long as extensive cerebral damage has not occurred.\textsuperscript{84}

Volatile agents such as halothane, methoxyflurane, and trichloroethylene produce dose-dependent increases in CBF, CBV, and ICP,\textsuperscript{45,129} accompanied by variable reductions in BP. Administration of high concentrations of these agents encourages brisk increases in

![Diagram of Intracranial Hypertension Pathophysiology]

FIG. 6. Pathophysiology of uncontrolled intracranial hypertension. Cycle elements potentially under the anesthesiologist’s control are indicated by asterisks.
ICP in patients with reduced compliance. Table 1 summarizes the pertinent physiologic trends that may be expected when volatile and other anesthetic agents are employed in neurosurgical practice. d-Tubocurarine causes an increase of ICP and reduction of CPP, presumably due to the vasodilating properties of histamine released by this agent. Following the pharmacologic establishment of muscle relaxation, ICP may decrease due to reduced central venous pressure and its cephalic transmission.

Hyperventilation, barbiturates, osmotic agents, and muscle relaxants employed prior to the introduction of volatile agents into the anesthetic bases may improve intracranial compliance and attenuate the increase of ICP caused by these inhalational agents. However, it should be realized that intracranial compliance cannot always be improved by these maneuvers. Their ICP-reducing action is directed toward healthy areas of brain with retained CO₂ responsiveness and an intact blood–brain barrier. Therefore, prior hyperventilation is most likely to prevent ICP elevation subsequent to the administration of a volatile anesthetic when the diseased area of brain is relatively small. With lesions not involving the brain stem, a normal level of consciousness is a reasonable indicator that more tissue retains normal vascular reactivity than does not. Hyperventilation is likely to fail when large areas of the brain are diseased, as with recurrent tumor, after an anoxic–ischemic episode, or with severe head injury in association with a diminished or absent level of consciousness. In these instances it is preferable to employ anesthetic agents that do not cause cerebrovascular vasodilation.

Initially, enflurane appeared to have a significant advantage over halothane because it was reported to have little effect on CBF at increasing levels of MAC. We have found significant ICP elevations or swelling of the brain in the operative field when enflurane was administered in the presence of normal or high arterial blood pressure and normal or reduced CO₂ tension. Probably the primary cerebrovasodilatory action of the volatile

<table>
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<tr>
<th>Technique</th>
<th>Blood Pressure</th>
<th>Intracranial Pressure</th>
<th>Cerebral Perfusion Pressure</th>
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<tr>
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<td>↑</td>
<td>↓</td>
<td>45</td>
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<td>↑</td>
<td>↓</td>
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<tr>
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<td>↓</td>
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<td>138</td>
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<tr>
<td>Pancuronium‖</td>
<td>−</td>
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* Clinically significant effects at commonly effective anesthetic or sedative doses are indicated. The resulting CPP direction of change depends not only on the BP and ICP directions but also on the magnitude of the change. Ventilation is assumed stable and controlled.

† Cerebral perfusion pressure = blood pressure – intracranial pressure.

‡ Halothane, methoxyflurane, fluoxene, enflurane.

§ Diazepam predicted from available CBF data.

¶ Pancuronium is assumed to be less potent in histamine-releasing properties than d-tubocurarine. Muscle relaxant effects in the table refer to actions immediately following their intravenous administration.
agents interferes with autoregulation and renders CBF and ICP blood pressure-dependent. Recent studies by Murphy et al. in normal man indicate dose-dependent CBF elevations during enflurane anesthesia when BP is maintained at normal levels.\textsuperscript{81} Similarly, Morita reports a progressive dose-dependent loss of autoregulation when halothane is administered to rhesus monkeys.\textsuperscript{85} It is likely that high concentrations of any volatile agent will modify or abolish autoregulation and render CBV more dependent on BP. Whether or not this results in a high CBF (associated with normal intracranial compliance) or an elevated ICP and cerebral ischemia (reduced intracranial compliance) depends on the overall or regional CPP.

Drug and disease interference with CBF autoregulation underscores the importance of simultaneously considering the levels and interactions of drug, $P_aCO_2$, $P_aO_2$, and blood pressure during neurosurgical anesthesia, and leads us to propose the ICP triad (fig. 7) as a basis for approaching the management of patients with elevated ICP. Application of this scheme requires simultaneous consideration of the major recognized factors contributing to intracranial homeostasis during anesthesia. For instance, vasopressor-induced arterial hypertension following a period of nitroprusside- or trimethaphan-induced hypotension results in marked intracranial hypertension despite an unchanged $P_aCO_2$.\textsuperscript{134} This could either be due to a persistent cerebrovasodilator action of the hypotensive drugs or be a result of cerebral acidosis occurring during the period of reduced CPP.

**OTHER ANESTHETICS ALTERING CEREBRAL BLOOD VOLUME**

Clinical doses of nitrous oxide are reported to increase ICP in patients with reduced compliance.\textsuperscript{36} However, as BP is maintained, CPP decreases will not be as great as those associated with the volatile agents. The ability of nitrous oxide to elevate ICP may be less than that of the other volatile agents, perhaps because of its sub-MAC dosage limitation.\textsuperscript{129} The potential for nitrous oxide to precipitate intracranial hypertension was not recognized until recently, since it was used as the control anesthetic to which a volatile agent was added. Such a protocol may bias the result against the volatile anesthetics, especially when equipotent doses are considered. For instance, there is no study describing the result of adding nitrous oxide to 0.6–0.7-MAC established halothane anesthesia.

Ketamine can quickly increase ICP, and often reduces CPP despite maintenance of normal or elevated blood pressures.\textsuperscript{122} The use of ketamine in neurodiagnostic or neurosurgical procedures should probably be avoided unless the fontanelles are open, a route for ventricular CSF drainage is available, and/or ventilatory control is maintained. Thiopental or passive hyperventilation can decrease the ICP elevation caused by ketamine,\textsuperscript{122} volatile agents,\textsuperscript{133} or nitrous oxide.\textsuperscript{26} This is probably due to a potent cerebral vasoconstrictor action.\textsuperscript{105} Frequently, thiopental not only reduces ICP but also improves CPP.\textsuperscript{112} Autoregulation is present during barbiturate anesthesia, whereas its functional status during ketamine administration is unknown.

The droperidol–fentanyl-relaxant technique can initiate a moderate decrease in ICP and, when used with nitrous oxide, provides an alternative to the volatile agents.\textsuperscript{26}

The cornerstone of neuroanesthesia in patients with or prone to develop intracranial hypertension centers on a smooth induction geared to improve intracranial compliance. This is probably best accomplished with hyperventilation (initially, voluntarily encour-
aged, if possible), thiob-arbitrurates, osmotic agents, and muscle relaxants. These maneuvers should improve the neurosurgical patient’s ability to compensate for subsequent intraoperative challenges to intracranial homeostasis, such as those associated with laryngoscopy and intubation, positioning, and subsequent administration of a volatile anesthetic.

**Intracranial Pressure Changes with Specific Lesions**

**Supratentorial Lesions**

The ability of the brain to compensate for an expanding lesion depends on the location of the lesion and its expansion rate, which in turn relate to the specific intracranial disease. Symptoms and signs of elevated ICP include headache, frequently associated with papilledema, nausea, vomiting, and behavioral changes, such as lethargy or drowsiness. During the preoperative review of the patient’s record, radiologic findings suggesting calvarium suture spread, increased convolutional marking (“beaten silver” skull erosion), thinning of the sella turcica, hydrocephalus, and shifts of intracranial structures should alert the anesthesiologist to the presence of intracranial hypertension.

**Tumors**

Typically slow expansion of these lesions allows major compensation to occur, provided early blockade of the CSF circulation does not occur. These patients may have large masses causing shifts in brain midline structures, accompanied by normal or moderately elevated ICP and markedly reduced intracranial compliance. Preoperative compliance tests may aid in identifying the especially high-risk patient, as well as provide a control for assessing the effects of anesthetic agents and techniques on ICP. Hemorrhage into the tumor bed of these patients usually results in marked intracranial hypertension and rapid neurologic deterioration.

**Hematoma**

With more rapidly expanding masses, such as acute epidural, subdural, or intracerebral hemorrhages, spatial compensation via CSF translocation may not occur rapidly enough to prevent an early local or generalized ICP elevation. Additional compensation may be provided by a reduction in CBV through compression of portions of the cerebral vasculature. This early vascular compromise may explain the rapid neurologic compromise associated with intracranial hematomas. More slowly-developing chronic subdural hematomas tend to follow the neurologic pattern established by the brain-tumor group.

Multiple injuries must also be considered in the patient with neurologic trauma. Shock, if present, further reduces CPP, and its correction takes precedence in the management of head injuries. Cervical neck fractures are commonly associated with head injury and must be considered in plans for airway control.

**Hydrocephalus**

The hydrocephalic state implies elevated amounts of CSF under increased pressure, the latter being present either currently or at some time in the past. The enlarged ventricles demonstrate that brain compression and/or a reduction in the subarachnoid space has occurred. With communicating hydrocephalus, the increased ICP is evenly distributed (little early brain distortion) and neurologic deterioration is delayed compared with that in patients with increased ICP caused by mass lesions. Hydrocephalic children undergoing repeated revisions of CSF shunts may have small scarred ventricles with markedly reduced periventricular compliance. They tolerate volume challenges to their intracranial compartments poorly, and their condition may deteriorate rapidly pre- or intraoperatively due to transtentorial and/or foramen magnum herniation. Respiratory obstruction causing stridor may occasionally be observed in infants with hydrocephalus and meningomyelocele several weeks after birth. The stridor may be alleviated after CSF-shunting procedure, and may be due to distortion and traction effects on the lower brain stem and cranial nerves.

The so-called “normal-pressure hydrocephalus syndrome” associated with dementia, incontinence, lethargy, and abnormalities of gait
in older individuals actually represents a subacute phase of hydrocephalus. Continuous recordings in these patients have revealed abrupt increases in ICP during sleep, associated with rapid-eye-movement dreaming or CO₂ retention. Therefore, one should not be misguided by the name of this disease when planning anesthesia for these patients.

**Subarachnoid Hemorrhage**

Concomitant with rupture of an intracranial aneurysm, ICP rapidly increases to levels approaching BP. This phase lasts only a few minutes and is thought by some to limit the amount of blood extravasated with rupture of the aneurysm. With repeated subarachnoid hemorrhages, the baseline level of ICP gradually increases due to accumulating clot, cerebral edema, and/or the immediate development of a noncommunicating (aqueductal) block. Later a communicating hydrocephalus may develop as blood hampers CSF flow through the basal cisterns or into the arachnoid villi. Prior to clipping of the aneurysm, efforts are directed toward preventing recurrence of hemorrhage by avoiding blood pressure elevations (sedatives and antihypertensive drugs) and in some centers by employing antifibrinolytic drugs (epsilon-aminocaproic acid) to prevent resolution of the intraneurysmal clot. An abnormal EKG suggesting myocardial ischemia, infarction, or arrhythmias may accompany subarachnoid hemorrhage. These changes are thought to be due to centrally mediated autonomic influences upon the myocardium, and it has been suggested that autonomic blockade might ameliorate this condition.

Progressive obtundation with subarachnoid hemorrhage accompanied by a rising ICP and hydrocephalus requires therapy directed toward reducing CSF production (acetazolamide, glycerol) or removal of CSF through an external ventriculostomy. In these cases, rapid normalization of the ICP, either in the operating room or in the intensive care unit, is to be avoided, since it may increase the transmural pressure gradient across the aneurysm wall and incite further hemorrhage. Here a moderately elevated ICP may actually protect the brain. Restitution of a cerebral perfusion pressure gradient of 60–80 torr seems a reasonable goal in these cases. Ventriculostomy with controlled CSF drainage in subarachnoid hemorrhage patients with deteriorating neurologic status, elevated ICP, and hydrocephalus can lead to significant improvements in preoperative condition. The presence of vasospasm preoperatively may contribute to the overall neurologic picture and should serve as a warning against overzealously treating arterial hypertension during induction of anesthesia, since cerebral ischemia is likely to occur in the cerebrovascular bed distal to the spasm.

**Benign Intracranial Hypertension (Pseudotumor)**

This syndrome, of uncertain etiology, consists of headache, papilledema, and increased ICP with normal or small ventricles in the absence of an intracranial mass. It most commonly occurs in young obese women, presumably on an endocrine basis, or it may follow steroid withdrawal, vitamin A intoxication, tetracycline administration, or intracranial venous sinus thrombosis. Surgical treatment may be necessary to achieve subtemporal decompression in an effort to prevent optic-nerve compression. Repeated lumbar taps for CSF removal, administration of steroids, and osmotic dehydrating agents may provide symptomatic relief.

**Infratentorial Lesions**

Measurement of the ICP in the posterior fossa is not commonly practiced. Infratentorial lesions are often accompanied by non-communicating hydrocephalus, and measurement of ICP from a lateral cerebral ventricle with or without controlled drainage of CSF can be easily accomplished. Frequently a CSF shunting procedure precedes definitive operations on the posterior fossa in an effort to remove the effects of intracranial hypertension. There is a general impression that this two-stage approach to lesions in the posterior fossa lessens the intraoperative complication rate. Although providing adequate control of the supratentorial pressure, shunting procedures do not protect the patient against the direct mass effect of the infratentorial lesion upon vital brain stem centers. Despite a low
supratentorial ICP recording, these patients must be observed carefully for the development of signs of respiratory and cardiovascular irregularities.

Pre- and postoperatively, special attention must be directed toward determining the status of the gag reflex and the ability of the patient to maintain his airway. When the neck is stiff, indicating possible tonsillar herniation, caution must be exercised in positioning the head for airway maintenance or tracheal intubation, since forceful anteflexion of the neck can initiate compression of the medulla, thereby precipitating cardiorespiratory failure.\textsuperscript{8,78}

**Neurologic Assessment**

Documented observation of neurologic status is the keystone of patient care in the neurologic intensive care facility and in the immediate preoperative period. Frequent determinations of neurologic status, chiefly concerned with changes in level of consciousness, gross motor responses, and brain-stem reflexes, are essential to determining the effects of therapy and/or the dynamic course of the intracranial disease. Communication of the temporal profile of neurologic function in the critically ill patient is probably best accomplished on a specialized neurologic status flow sheet.\textsuperscript{9}

**LEVEL OF CONSCIOUSNESS**

Plum and Posner have developed a useful format for the evaluation of patients who have neurologic abnormalities in a critical care environment.\textsuperscript{107} With a slowly expanding supratentorial lesion, neurologic signs tend to progress in a rostral-to-caudal sequence, \textit{i.e.}, from the higher cerebral centers to lower brain stem functions. Accordingly, changes in level of consciousness are the most important signs of deteriorating neurologic condition. These changes in levels of consciousness may be classified according to the outline in table 2.

Coma can result from expansion of a supratentorial mass lesion, a discrete reticular formation lesion, or metabolic depression of either the cerebral or the reticular activating formation.\textsuperscript{107} Discrete reticular formation lesions usually have associated brain-stem abnormalities and tend to remain static. Cerebral metabolic depression associated with congestive heart failure, electrolyte imbalance, and endogenous or exogenous toxins is accompanied by few focal signs (in the absence of previous brain disorders) and preservation of brain-stem reflexes.\textsuperscript{107} With an expanding supratentorial lesion, focal and generalized neurologic dysfunction in a rostral-caudal progression occurs as first the cerebral hemispheres and then the brain stem become progressively involved in the tissue-distorting process.

Ventilatory pattern abnormalities may indicate the level of progression of disease through the central nervous system. However, they are in themselves not sufficient to localize CNS lesions, since Cheyne-Stokes respirations accompany a number of cardiopulmonary abnormalities,\textsuperscript{107} as well as brain dysfunction due to increased ICP.\textsuperscript{107} Additionally, central neurogenic hyperventilation may be the result of a pontine lesion,\textsuperscript{107} systemic hypoxia,\textsuperscript{95,106} or metabolic acidosis.

**Table 2. States of Altered Consciousness Based upon a Stimuli-and-response Format**

<table>
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<tr>
<th>Usual Description</th>
<th>Stimulus</th>
<th>Response</th>
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<tr>
<td>Alert</td>
<td>Normal, discontinuous, internal or external</td>
<td>Immediate, complete, appropriate</td>
</tr>
<tr>
<td>Lethargic</td>
<td>Enhanced, discontinuous, external</td>
<td>Delayed, incomplete, appropriate</td>
</tr>
<tr>
<td>Obtunded</td>
<td>Enhanced, discontinuous, external</td>
<td>Barely maintains wakefulness</td>
</tr>
<tr>
<td>Stupor</td>
<td>Vigorous, continuous, external</td>
<td>Maintains wakefulness only with continued stimulus, inappropriate</td>
</tr>
<tr>
<td>Coma</td>
<td>Vigorous, continuous, external</td>
<td>No psychological or motor response, * reflexes</td>
</tr>
</tbody>
</table>

\* reflexes
**BRAIN-STEM REFLEXES**

When consciousness is lost, further neurologic evaluation focuses on brain-stem function. Observation of a few brain-stem reflexes and functions permits assessment of the continued caudal progression of the intracranial disease process. ICP measurement improves our overall ability effectively to manage patients who have neurologic disorders, but does not replace the neurologic examination.

Evaluation of brain-stem reflexes includes: 1) pupil size and reactivity; 2) respiratory pattern; 3) oculovestibular reactions (tested by the doll’s eyes maneuver or caloric stimuli); 4) the pattern of motor reactions to painful stimuli. These observations permit one to approximate roughly the level of brain-stem function remaining during the caudal progression of the disease process. They are illustrated in figure 8 and discussed below.

Midbrain compression is associated with pupillary abnormalities progressing from a loss of light reactivity (Edinger-Westphal nucleus) to complete oculomotor palsy caused by transtentorial herniation and compression of cranial nerve (CN) III. The oculovestibular reflex is intact during early midbrain compression. It involves the interconnection of the CN-III nucleus in the midbrain and CN-VI and CN-VIII nuclei (located at the pontomedullary junction) through the pons via the medial longitudinal fasciculus (MLF). Caloric stimulation is the preferred method in testing the oculovestibular response for several reasons: 1) vigorous head movements required by the doll’s eyes maneuver in patients with head injuries may be dangerous due to the high
incidence of associated fractures of the cervical spine; 2) head movement may accelerate tracheal damage in intubated patients; 3) caloric elicited responses are more easily observed and quantitated. To elicit the oculo-vestibular reflex 20–100 ml of iced saline solution are flushed into the ear canal with the head elevated to 30 degrees above the horizontal axis, after examination of the ear canal and drum (for obstructing cerumen or ruptured drum). A normal response consists of conjugate deviation of the eyes toward the side of the cold stimulus. See Plum and Posner for further details.\textsuperscript{105}

With increased midbrain involvement the oculomotor (CN-III) component is lost, and only ipsilateral disconjugate lateral deviation of each eye occurs (CN-VI and CN-VIII intact). Direct compression of CN-III by herniating brain produces a complete ipsilateral oculomotor palsy. The patterned motor response progresses from decortication to decerebration. Hyperthermia frequently occurs as the hypothalamus becomes involved.

Progressive involvement of the midbrain changes the respiratory pattern. Classically, hyperventilation has been associated with midbrain lesions.\textsuperscript{95,106,107} It now appears that true cases of central neurogenic hyperventilation associated with midbrain lesions must occur very rarely, if ever.\textsuperscript{106} Hypoxia associated with intracranial abnormality probably causes the associated tachypnea.

Progression through the pons is documented by changes in the pattern of respiration from the regular pattern of central hyperventilation to irregular patterns of cluster or apneustic breathing as respiratory coordinating centers are interrupted. Gross irregularities in breathing localize the brain lesion caudal to the midbrain level.\textsuperscript{95} With low pontine lesions flaccidity develops and the oculo-vestibular reflex is abolished.

Compression of the medullary cardiovascular and respiratory centers constitutes the last stage of compression of the brain due to an expanding intracranial mass. Ataxic respirations and cardiovascular instability characterized by hypertension and tachycardia may precede or replace the development of the classic Cushing triad (intracranial hypertension, bradycardia, and arterial hypertension). Apnea and a decreasing blood pressure constitute the terminal event.

**Specialized Monitoring**

**ICP Measurement**

Treatment of intracranial hypertension in the individual patient is most rationally approached when the ICP is monitored.\textsuperscript{12,48,56,141} In several centers the use of ICP levels to determine ultimate prognosis for patients who have sustained head injuries has met with variable results.\textsuperscript{12,48,138,141} Troupp suggests that ICP levels above 60 torr are indicative of a very poor prognosis.\textsuperscript{109} The pattern of ICP fluctuations as recorded over 24 hours may also yield useful prognostic data.

ICP monitoring has evolved in two major directions, including either systems that involve a fluid-coupled external transducer or systems requiring intracranial implantation of a small electronic transducer. Implanted transducers have been fraught with technical problems relating to calibration and system stability over prolonged periods. Since the average duration of ICP measurement in our institution is approximately five days, this constitutes a severe problem. One commercially available system employs an external transducer servo-coupled to a pressure-sensitive switch, which is placed epidurally.\textsuperscript{96}

Perhaps because the transducer is readily available for recalibration and zero determination, fluid-coupled external transducer systems have received the widest clinical application. The most popular method, as developed by Lundberg, consists of placement of a catheter in a lateral cerebral ventricle.\textsuperscript{98} This permits both pressure monitoring and therapeutic drainage of CSF. The difficulties associated with this method are problems in catheterizing a ventricle in the presence of swelling and distortion of the brain, accidental venting of CSF, and infection. A promising new method for monitoring ICP in the subarachnoid space involves threading a small hollow bolt into the skull so that its tip lies below the opened dura.\textsuperscript{142} The system is then connected through a short length of tubing to a transducer. The hollow bolt is easily placed; however, CSF drainage cannot
be performed through it, and infection remains a possibility.

A Millipore filter connected to the ventricular catheter or the subarachnoid bolt impedes intracranial contamination and permits excellent transmission of pressure patterns. Since trends over periods ranging from hours to days are important in ICP management, the ICP, BP, and other pressures are recorded on a polygraph after passing through a suitable alarm circuit. All pressures are zeroed at heart level to facilitate computation of CPP. It is advantageous to connect a small transducer to the fluid-coupled system in a manner that permits it to be incorporated within the head dressing. This will obviate artifactual recording of ICP due to changes in the position of the patient. Figure 9 shows the system we employ for ICP measurement from the subarachnoid screw or ventricular catheter. In some facilities patients undergoing ICP monitoring are prophylactically given antibiotics.

**CBF Measurement**

Frequently a complex clinical situation arises where it becomes necessary to balance the blood pressure against ICP and CPP generated by an arterial pressure head. The measurement of CBF employing isotope-clearance techniques can aid in determining this blood pressure set point, as well as aiding in other diagnostic and management problems.

Cerebrospinal fluid can be measured in the critical care setting by monitoring the clearance of a gamma-emitting radioactive isotope, usually $^{133}$Xe, with external scintillation counters after injection of the tracer into the internal carotid artery. On-line computer analysis of the clearance curves is usually performed. Manual analysis of the slope of isotope washout during the initial 2 minutes of clearance provides an index of flow in the grey matter. Repeat studies necessitate recurrence of the cerebral vasculature or leaving the original catheter near, or within, the internal carotid artery. The hazard of emboli arising from this catheter limits the applicability of the intra-arterial CBF measurement technique for repeat studies.

Recently, regional CBF measurements have been performed with external scintillation counting after inhalation or intravenous injection of $^{133}$Xe. This technique is based upon the use of end-tidal $^{133}$Xe measurements to provide an estimate of arterial recirculation of the tracer and an extensive computer analysis of the raw data. The intra-arterial injection and inhalation techniques require that a stable physiologic state exist for 15 to 40 minutes (longer period for slow CBF) in order to complete the study. Recently, Obrist and colleagues refined the inhalation technique to provide an index of grey-matter flow within 10 minutes. Difficulties with the inhalational method occur when CBF is very low due to the inability to separate the normally low extracranial cephalic blood flow from the now-reduced intracranial flow. Although a promising addition to neurovascular monitoring, the noninvasive CBF measurement technique is yet in its developmental stages, and validation by comparison with the intra-arterial method is needed.

Catheterization of the internal jugular vein when CBF measurements are performed permits determination of the cerebral meta-
bolic rates for various substrates. This may be accomplished by retrograde catheterization of the internal jugular vein or transverse sinus, or by direct puncture of the internal jugular vein or jugular bulb. Measurement of CBF and cerebral metabolism may provide prognostic indices in management of patients who have head injuries, as well as guide therapy directed toward maintaining a match between metabolic demands and CBF.

OTHERS

Continuous electroencephalography coupled with small on-line processing units for EEG spectral array display and equipped with alarms may provide yet another valuable noninvasive monitor for the neurologic patient. Echoencephalography permits determination of midline shifts in patients with supratentorial masses and can easily be performed at the bedside. Although not physically situated within the neurologic intensive care unit, the newly introduced axial computerized tomographic scanner (EMI transmission brain scan) is a powerful adjunct in the care of patients with intracranial disease. The scan is totally noninvasive, requires 20 minutes to complete, and renders information concerning ventricular size, presence of extravascular blood, cerebral edema, infarcted brain, tumor location, and position of midline structures.

Management of Intracranial Hypertension

STABILIZATION AND COMA CARE

The first one to two days after a cerebral insult represent the stabilization period for most patients who have neurologic disorders. Provided a secondary brain insult does not occur, cerebral swelling tends to be maximal 24–48 hours following an injury. This period is often interrupted by diagnostic, surgical, and other procedures, and frequently neurologic worsening accompanies these events. Shock due to delayed traumatic or steroid/stress-induced gastric hemorrhage may occur, and its correction is pre-eminent. Electrolyte imbalance and water depletion may develop consequent to aggressive ICP-reduction therapy. Hyperosmolality can in itself cause coma or the development of focal neurologic signs. It may confusingly retard neurologic recovery when it occurs rather late in the clinical course, and is likely to occur following inadequate rehydration after aggressive dehydration therapy coupled with a continuing steroid-induced hyperglycemic osmotic diuresis.

Nasogastric suction is frequently required for comatose patients. However, in the absence of adequate airway protection it increases the incidence of aspiration pneumonitis. Instillation of antacids into the nasogastric tube may serve the dual function of reducing the incidence of gastric ulceration and limiting the severity of acid-induced pneumonitis should aspiration occur. The presence of a cuffed endotracheal tube may not prevent repeated episodes of pulmonary soiling associated with tube feedings. In this situation intravenous hyperalimentation or a gastrostomy may provide alternatives for the maintenance of adequate nutrition.

Although it is commonly recognized that elevation of the patient’s head above the horizontal plane will reduce cerebral venous and intracranial pressures (fig. 10), it is not widely appreciated that small changes in the position of the head and neck can greatly alter cerebral venous volume. Figure 10 also indicates that the magnitude of these changes relates not only to head and neck relationships, but also to the prevailing level of ICP. Venous pressure changes assume greater importance when intracranial compliance is reduced. Paradoxically, with very high intracranial pressures (those approaching the arterial pressure level), even bilateral jugular compression has little effect on ICP, presumably because CBF is markedly reduced.

Recently, percutaneous puncture of the internal jugular vein has been advocated as a means of rapidly establishing a central venous route for fluid administration or pressure monitoring. To prevent air embolism during introduction of the catheter, it is suggested that the patient be placed in the head-down position. At the time of puncture a voluntary Valsalva maneuver or moderate airway pressure in intubated patients has been used to increase venous blood reflux back into the catheter. In one patient subjected
to increased airway pressure, the ICP (15 to 120 torr) and systemic cardiovascular changes (110 to 160 torr) provoked by this technique summated to produce a mean CPP of approximately 40 torr for more than a minute. When percutaneous jugular catheterization is necessary in patients with elevated ICP, it should be performed using suction on the syringe rather than maneuvers designed to increase intrathoracic pressure.

**Respiratory Care**

Appropriate management of the airway and ventilation is vitally important in managing patients with intracranial abnormalities. If there is any doubt regarding the ability of the patient to maintain his own airway, endotracheal intubation is mandatory. Not infrequently, intubation will be necessary for less than 24 hours in patients with head injuries who have severe CNS concussion. Provision of an adequate airway during this period may prevent untoward complications.

The restless comatose patient presents a special problem with regard to endotracheal intubation. At times, sedatives, narcotics, and/or muscle relaxants are needed to suppress head thrashing and arterial hypertension due to the stimulus of the tracheal tube. We rely primarily on muscle relaxants in this situation, and add small doses of phenothiazines, lidocaine, iv, 50, 106 and short-acting narcotics to block noxious laryngeal stimuli and to control arterial hypertension. The neurologic examination can be partially obscured by these drugs, and their use is coordinated with the neurosurgeon’s protocol for immediate management. Whenever possible, we avoid employing narcotics (which cause miosis) until the diagnosis and the expected course of the disease have been established. Early employment of ICP monitoring in these situations greatly aids management when the development of mass lesions such as intracranial bleeding or cerebral edema is anticipated.

**ICP Increases Due to Therapy:** Intracranial hypertension, at times sustained and associated with neurologic deterioration, may be initiated by respiratory care and nursing maneuvers. 69, 124 These adverse ICP responses may be caused by transmission of increased intrathoracic pressure to the cerebral venous system, direct pressure on the jugular veins, and/or arterial hypertension. An arousal response, due to tracheal toilet or other intense stimuli, may also cause increases in CBV. 113

Personnel administering respiratory therapy and other nursing duties should be aware of these problems. Treatments should be timed to take advantage of periods of maximum sedation and muscle relaxation. ICP measurements in patients given respiratory therapy in our unit indicate that in most patients these treatments are not harmful. However, in some instances IPPB or hyperinflation...
therapy may have no significant effect on ICP at one stage of a disease process, while the same treatment given later may elicit a marked elevation of ICP.

Despite already established hyperventilation, endotracheal suctioning in anepic paralyzed patients is accompanied by CO₂ accumulation, which can cause significant increases in ICP (fig. 11). In this circumstance the PₐCO₂ increases by about 10 torr during the first minute of anepa in our patients. Arterial hypertension, if it accompanies the suction stimulus, may then further augment this ICP elevation. Once tracheal or other stimuli elicit an ICP increase the newly established level of intracranial hypertension can persist despite reinstitution of therapy that had previously controlled the ICP. An example of this is the persistently higher ICP after arrow 4 in figure 11. Chest-percussion physiotherapy appears to cause minimal ICP increases unless arterial hypertension accompanies it.

The occurrence of dangerous levels of ICP following a nonspecific stimulus is largely unpredictable in regard to its onset; however, once observed, precipitous intracranial hypertension can be expected to recur when similar challenges are presented. Personnel administering respiratory care and other nursing requirements should observe the ICP when possible and modify their ministrations appropriately. In the absence of ICP monitoring, prolonged pressurization of the airway and painful stimuli should be minimized.

While potential problems relating to the administration of respiratory and nursing care to patients with intracranial hypertension are becoming more widely recognized, the actual benefit-to-risk ratio for each patient remains undetermined, and therapy must be individualized. Pretreatment with moderate doses of thiopental prior to tracheal suctioning in patients who have reactive intracranial hypertension has proved helpful in some instances, but is not a general panacea. Attention is currently being directed to other means of modifying potentially harmful ICP responses. These include extreme elevation of the head of the bed when continuous positive end-expiratory pressure (PEEP) is required, gradual reduction of PEEP prior to venting to atmosphere to prevent an abrupt elevation in blood pressure associated with suddenly augmented venous return to the heart, and topical anesthesia of the tracheal mucosa prior to suctioning. Further studies of the complex interaction of respiratory care and ICP should simultaneously consider intracranial compliance, the state of cerebral blood flow autoregulation, PₐCO₂ levels and changes, and the rate and extent of changes in cardiovascular variables.

Neurogenic Pulmonary Dysfunction: Hypoxemia is frequently present in patients who have neurologic disease. When pulmonary complications associated with hypostatic or infectious pneumonia, aspiration pneumonitis, chronic cardiac failure, and fluid overload are removed from consideration, there exists a body of experimental and clinical data indicating that severe respiratory dysfunction can be the result of neurogenic factors. 5,7,21,22,32,36,85-89

These may range from severe pulmonary edema occurring within 2 hours of abruptly elevated ICP in young head-injured patients without prior cardiopulmonary disease to progressive widening of the alveolar-arterial
oxygen gradient in patients who have sustained severe head injuries. This less fulminant process may be accompanied by variable clinical signs of pulmonary edema and a decreased carbon-monoxide-diffusing capacity. Frank pulmonary edema occurring in concert with intracranial hypertension is generally refractory to cardioactive and diuretic drugs, and becomes tractable after intracranial decompression. PEEP appears to be the most successful means for maintaining oxygenation until intracranial decompression can be effected. In several clinical series, severe arterial hypoxemia, present or developing soon after admission of patient who had sustained neurologic trauma, was associated with neurologic worsening or a grim ultimate prognosis.

The mechanism(s) responsible for eliciting a neurogenic form of pulmonary edema are not clearly established. Central nervous system lesions involving the hypothalamic preoptic nuclei or the medulla have been shown to cause sudden increases in central blood volume due to intense peripheral vasoconstriction, leading to acute left heart failure. Hypothalamic linked sympathetic discharges have also been implicated as causing elevated pulmonary capillary bed pressure, perhaps by inducing venular spasm. Acute mechanical head injury in unanesthetized rats produces immediate onset of fulminant pulmonary edema associated with decreased lung compliance and reduced surfactant. In a number of species these changes can be produced by appropriate stimulation in the absence of CNS disease, and the responses to such injury and electrical stimulation are mitigated by prior anesthesia and adrenergic blockade. A trial of alpha-adrenergic blockade did not alleviate hypoxemia in one clinical series of patients who had sustained head injuries. Species differences in the expression of neurogenic pulmonary dysfunction exist. Mechanical brain injury or stellate-ganglion stimulation in squirrel monkeys decreases pulmonary compliance without the concomitant abnormalities indicative of overt pulmonary edema found in rats subjected to the same insult.

Experimentally, a generalized abrupt elevation in ICP can also initiate arterial hypoxemia and signs of pulmonary edema. This is associated with a generalized vasopressor response and pulmonary venous hypertension, and is prevented by cervical cord section. Isolated pressure upon the floor of the fourth ventricle and thoracic or cervical spinal cord produces similar hemodynamic responses and suggests that diffusely increased ICP may stretch or exert pressure upon receptive elements located in the hypothalamus or brain stem. In lightly anesthetized dogs progressive ICP elevation leads to parallel increases in pulmonary venous admixture. Development of this pulmonary shunting occurs with a short latency (5–10 minutes) and reverses within a similar period when intracranial hypertension abates. Increases in cardiac output can accompany these changes, suggesting that overdistention of the pulmonary vascular bed may contribute to alveolar collapse and shunting. Other work in dogs, using an open-chest pump-perfused preparation subjected to increased ICP, supports the foregoing study in that no significant primary alteration in pulmonary vascular resistance was found despite the presence of an intact systemic vasopressor response.

It has been suggested that the so-called "shock-lung syndrome" and neurogenic pulmonary edema may share a common etiologic basis. Moss and associates believe that shock lung is the result of spasm in small pulmonary venules, initiated by hypothalamic hypoxia occurring during shock. Selective cerebral vascular perfusion with blood at $P_{O_2} = 35$ torr caused pulmonary congestion, interstitial edema, and intraalveolar fluid accumulation despite maintenance of normal systemic oxygenation. Further support for neurogenic factors influencing pulmonary capillary water exchange comes from the work of Sugg, who found that removal and reimplantation of one lung prior to hemorrhagic shock provided protection against shock lung. In another study Kusajima et al. induced an isolated reduction of cerebral perfusion pressure to 35–40 torr and did not observe significant alterations in pulmonary vascular pressures or disorders of the lung. While this perfusion pressure may not be sufficient to cause hypothalamic ischemia, the
TABLE 3. Etiologic Classification of Intracranial Hypertension States and Treatments Specific to Them

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Intracranial mass</td>
<td>Surgical removal</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>Fluid restriction</td>
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<tr>
<td></td>
<td>Diuretics</td>
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<tr>
<td></td>
<td>Osmotic</td>
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<tr>
<td></td>
<td>Tubular</td>
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<td></td>
<td>Steroids</td>
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<td></td>
<td>Hyperventilation</td>
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<td></td>
<td>Hyperthermia</td>
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<tr>
<td></td>
<td>Barbiturates</td>
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<tr>
<td></td>
<td>Controlled hypotension</td>
</tr>
<tr>
<td></td>
<td>Surgical decompression</td>
</tr>
<tr>
<td>Increased intravascular blood volume</td>
<td>Position</td>
</tr>
<tr>
<td></td>
<td>Hyperventilation</td>
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<tr>
<td></td>
<td>Blood pressure stability</td>
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<tr>
<td></td>
<td>Muscle relaxants</td>
</tr>
<tr>
<td></td>
<td>Barbiturates</td>
</tr>
<tr>
<td>CSF retention</td>
<td>Osmotic agents</td>
</tr>
<tr>
<td></td>
<td>Reduction of CSF formation</td>
</tr>
<tr>
<td></td>
<td>CSF shunting procedure</td>
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same investigators found evidence of small-pulmonary-vein constriction during hemorrhagic hypotension, supporting Moss’ thesis.

While there is much to suggest that there is a brain–lung relationship relating to pulmonary function, the physiologic substrate mediating neurogenic pulmonary dysfunction is not clearly understood. Part of this confusion is probably due to species differences, lack of anesthetic control between laboratories, and technical difficulties in ascertaining specific changes in blood volume and water content in the lung. Additionally, the ability of the lung to respond to diverse challenges is probably quite limited, with the expression of end-stage pulmonary disease being quite similar despite different etiologies of lung dysfunction.

**Specialized Therapeutic Procedures**

The ability of the neurointensive care team to monitor variables relevant to brain function greatly enhances application of specialized methods of treatment. Techniques for reducing ICP should be directed toward the etiologic factors inciting the pressure increase, as noted in table 3. Selective application of these treatments frequently results in dramatic reduction of intracranial pressure, often accompanied by clinical improvement.

**Acute Intracranial Hypertension and Herniation Syndromes**

Incipient or recently established herniation of the brain may be quickly aborted or reversed by a combination of hyperventilation, mannitol (1–2 g/kg), and furosemide. When it is effective, hyperventilation provides an almost immediate intracranial hypotensive action. CSF pressure usually begins to decrease within 10–15 minutes after administration of osmotic agents and diuretics. A combination of mannitol, furosemide, and hyperventilation may be required to gain time to perform emergency neurodiagnostic procedures or a definitive emergency surgical procedure. This therapeutic combination is directed not at the etiologic cause of the increased ICP per se, but rather at the volume reduction of any responsive intracranial component. While it will not reduce the volume of extravasated blood, which requires surgical decompression, it can transiently arrest dangerous intracranial shifts until the mass is evacuated or the diagnosis established.

**Cerebral Edema**

Cerebral edema is defined as an increase in the water content of the brain. Usually it is accompanied by transudation of serum proteins across an abnormally functioning blood–brain barrier (BBB), and for this reason it has been called “vasogenic cerebral edema.” Clinically it commonly accompanies cerebral trauma, inflammatory disease, brain tumors, ischemic necrosis, or hypertensive encephalopathy. Therapy is directed at dehydra tion of the brain, promoting BBB restitution, and preventing secondary cerebral ischemia or hemorrhages due to intracranial hypertension. Experimentally, BBB recovery appears to require approximately 48 hours, and once re-established, the effects of osmotic agents and normal mechanisms of the brain for restoring cerebral fluid balance should be enhanced.
Cerebral edema can be clinically encountered without alteration in BBB. One example of this type of edema may be classified as osmotic cerebral edema, and can occur with water intoxication or when osmolality in the brain exceeds serum osmolality, as in the case of hyperosmolar hyperglycemic nonketotic coma.\textsuperscript{79} Pseudotumor cerebri (discussed above) apparently also occurs in the presence of a normal BBB to serum proteins.

**Diuretics and Water Restriction:** The use of hypertonic non-electrolyte solutions for the rapid removal of water from brain tissue was introduced by Javid in 1958.\textsuperscript{43} These agents are powerful adjuncts in the management of intracranial hypertensive states. Not only do they decrease an elevated ICP, but they can increase CBF, at times even before their intracranial hypotensive action is recognized.\textsuperscript{13} Requirements for the ideal osmotic diuretics for use in neurologic patients are: 1) trans-vascular passage into the brain impeded by the blood–brain barrier; 2) freely filterable at the glomerulus; 3) limited renal reabsorption; 4) otherwise pharmacologically inert. Pappius and colleagues have shown that therapy with a hyperosmotic agent dehydrates normal brain without removal of sodium and has no direct effect on edematous areas of cerebral tissue situated within an area of defective blood–brain barrier.\textsuperscript{102} Studies in nephrectomized monkeys have shown that the initial hypotensive action of hypertonic agents on ICP is independent of diuresis.\textsuperscript{44}

Intravenously administered urea was originally employed to establish an osmotic gradient between brain and blood for the regulation of ICP.\textsuperscript{43} Urea has been largely supplanted by mannitol because urea penetrates the blood–brain barrier at a much greater rate (smaller molecular size), has a shorter duration of action, is significantly reabsorbed by the renal tubules, and is more of a vascular irritant. Mannitol may be administered as a dilute intravenous infusion (20 per cent, 2.5–3 g/kg, over 1 to 1.5 hours)\textsuperscript{146} or given more rapidly (1–1.5 g/kg iv over 10 minutes) when acute neurologic deterioration is present. Hypertonic agents must be used cautiously in the presence of congestive heart failure, since transient intravascular hypervolemia accompanies their use.\textsuperscript{85,145}

There is much controversy regarding a rebound or secondary overshoot in ICP following the use of hypertonic agents to reduce intracranial hypertension. While these agents slowly penetrate the blood–brain barrier under normal circumstances,\textsuperscript{146} they probably enter the brain more rapidly when blood–brain-barrier function is disrupted. Therefore, they potentially could increase osmolality of the brain and pull water back into the brain when plasma concentrations of the osmotic agent decrease. Experimentally, ICP rebound can be prevented by limiting volume replacement to a third of that lost during the osmotic diuresis caused by either urea or mannitol.\textsuperscript{35} This indicates that the so-called "ICP rebound" may be dependent on the state of total-body hydration. Under similar conditions simultaneous administration of steroids appeared to preserve the ICP hypotensive effect of mannitol.\textsuperscript{39} Similarly, administration of ethacrynic acid just before mannitol infusion potentiates both the rate and the duration of ICP decrease in animals with cerebral edema.\textsuperscript{145} Tubular diuretics alone promote diuresis but have little acute intracranial decompressive action.\textsuperscript{145} However, furosemide has recently been shown to reduce the amount of subsequent cerebral edema in cats and monkeys following a freezing lesion.\textsuperscript{14,63} A small clinical study suggests that the immediate preoperative use of mannitol coupled with relative water restriction limits the commonly observed second-day-postoperative increase in total-body water.\textsuperscript{127}

More chronic ICP reduction therapy may be achieved with oral administration of hypertonic agents such as glycerol\textsuperscript{90} or isosorbide.\textsuperscript{66} The oral route is most commonly employed for treatment of cerebral edema due to vascular occlusion, pseudotumor cerebri, and hydrocephalus. Oral osmotic agents have been employed with variable success to tide infants over a period prior to an initial CSF shunting procedure or in cases when a shunt is removed because of an infectious process.\textsuperscript{66} The chronic use of hypertonic agents, especially in infants, is often accompanied by electrolyte disorders and an increasing BUN. When intracranial bleeding is suspected, these agents must be employed with extreme caution, since they may shrink healthy brain tissue and encourage
expansion of an intra- or extracerebral hematoma.29 In older patients sudden reduction of brain size may rupture the fragile veins entering the sagittal sinus, resulting in a subdural hematoma.73

We have observed two cases in which continuous administration of very high doses of mannitol (more than 10 g/kg/day was used for more than three days in an effort to control ICP. These patients developed serum osmolalities of more than 350 mOsm, accompanied by isosmotic urine and increasing serum K+. During attempts to reduce serum hyperosmolality in one of these patients with either isotonic saline solution or peritoneal dialysis, a rebound type of intracranial hypertension occurred. Presumably this occurred because brain-tissue osmolality had risen above the osmolality of the dialysate or infusion fluid.

Moderate preoperative water restriction (serum mOsm range 300–320) combined with diuretics, continued water restriction, and obligatory loss of urine due to steroid-induced hyperglycemia, necessitates continued clinical vigilance to avoid severe electrolyte and fluid imbalance. Measurement of serum and urinary osmolalities and electrolytes and careful replacement of fluid loss with appropriately tailored solutions are necessary to manage the complex metabolic problems associated with aggressive pharmacologic intracranial decompressive therapy.

Steroids: Since their introduction into neurosurgical practice around 1960,28,55 steroids have become one of the agents most frequently prescribed for combating cerebral edema. Their beneficial effects in patients with cerebral edema due to primary or secondary brain tumors and pseudotumor are established. Less certain is their efficacy in thrombotic or embolic strokes.54,104 Their usefulness in clinical management of head injury remains equivocal.118 The mechanism(s) by which steroids decrease cerebral edema is unknown. It has been suggested that they may protect the BBB, prevent lysosomal enzyme activation, enhance cerebral electrolyte metabolism, increase brain energy supplies (glucose) and/or promote water and electrolyte excretion.10,156,158

Steroids will not achieve rapid reduction of ICP, and are thereby dissimilar from hyper-ventilation or osmotherapy. However, within hours they may improve the neurologic condition of patients with intracranial neoplasms complicated by cerebral edema.114 Electron microscopic studies of biopsy specimens obtained from patients with various intracranial diseases suggest a reduction in cerebral edema in those pretreated with dexamethasone.85

Experimentally, steroids have been shown to reduce cerebral edema formation and retard its subsequent spread through the white matter when given to animals prior to head injuries of various types.53,115 Since our concept of continued neurologic deterioration after head injury implies the progressive incorporation of healthy tissue into a pathologic cycle, we administer steroids preoperatively and after head injury, hoping to afford protection to the tissue around the lesion.

The difficulty in interpreting studies purporting to show an effect of steroids on cerebral edema is pointed out in a recent experiment employing an infarction model.43 High-dose dexamethasone therapy continued for 48 hours after infarction limited entry of plasma protein into necrotic tissue but had no effect on protein penetration into the peri-infarctional ischemic tissue. This demonstrates the necessity for precise definition of tissue status and sampling sites in studies of experimental cerebral edema. The finding that steroids restricted plasma protein accumulation in necrotic tissue indicates a possible mechanism whereby they may offer some protection against increased ICP92 by reducing the total colloid osmotic pressure of the infarcted area.

Surgical Decompression: One of the dangers inherent in employing powerful pharmacologic decompressant therapy is the danger of masking a lesion for which the only definitive treatment is surgical. Whenever extremely large doses of mannitol are needed to maintain a reduced ICP, re-evaluation of the intracranial disease process is necessary. This applies even after operation. In some instances this may necessitate further neuroradiologic diagnostic studies while the patient remains under intensive care.

Hyperventilation: When a combination of osmotherapy and steroids does not accomplish sufficient intracranial decompression, hyperventilation therapy is usually the next step.
If coma is deep and a tracheostomy provides the airway, muscle relaxants are generally not used. This permits clinical assessment of neurologic status. When endotracheal intubation provides the route for hyperventilation, as is usually the case with acute head injury, we feel that use of muscle relaxants potentiates the action of hyperventilation in reducing intracranial blood volume (see below). While it appears that CO₂ reduction therapy is directed at areas of brain maintaining relatively normal cerebrovascular reactivity, hyperventilation therapy may also provide a sink for hydrogen ions generated by the disease process. This action may serve more rapidly to restore vascular reactivity to CO₂ in recovering tissue. More than 50 per cent of patients who have sustained severe head injuries will be spontaneously hyperventilating and will not require additional ventilation unless they show signs of increasing ICP. In some institutions passive hyperventilation to PaCO₂ levels of 25–30 torr is performed in management of all patients who are comatose following trauma with apparent improvement in overall mortality rates. However, there is no consensus as to whether this treatment returns more patients to an independent social existence. Since CSF pH and CBF normalize after several days of hypocapnia in normal man, continuous hyperventilation to a fixed PaCO₂ may actually provide intracranial hypotension with decreasing efficacy as its use is prolonged.

Other Methods for Treating Cerebral Edema: Hypothermia has been employed to reduce intracranial tension in a variety of clinical situations. It carries with it the need for respiratory support, the need for drugs to reduce shivering, the danger of cardiac arrhythmias, and a number of other complications. Despite laboratory evidence that hypothermia reduces CBV and brain water and directly blocks the development of cerebral edema in laboratory animals, its clinical use has largely been abandoned. This has been done on the basis that its risks far outweighed its somewhat vague clinical advantages. These impressions regarding its usefulness were largely formulated prior to the development of modern intensive care units and objective means of monitoring its effect on ICP. Currently, moderate hypothermia, alone or in combination with drugs that have anti-edema actions, is undergoing re-evaluation. Certainly hypothermic therapy directed at the reduction of hyperthermia should not be withheld, since elevated temperatures increase cerebral metabolism and the formation of cerebral edema.

Experimentally, barbiturates have been shown to afford the brain some protection against anoxia, ischemia, and vasogenic cerebral edema. These effects may be mediated either through reduction in cerebral energy requirements or via an action on the cerebral collateral circulation. Arterial hypotension, which may be directly induced or may accompany hypothermia and/or high-dose barbiturate therapy, also reduces the formation of vasogenic cerebral edema following a cortical freezing lesion. Hypertension, on the other hand, has been shown to augment cerebral swelling rapidly when autoregulation is disturbed. Reserpine can cause reductions in both body temperature and blood pressure and diminish experimental cerebral edema. The authors postulate that its beneficial effect may also be due to serotonin depletion, as this neurotransmitter initiates cerebral edema upon injection into the brain.
Clinical experience relating to reduction of cerebral metabolism and control of blood pressure to prevent or treat cerebral edema remains fragmentary. In centers with special interests in neurologic intensive care, these treatments should be considered when there is evidence that progressive intracranial hypertension resistant to the more commonly accepted therapeutic modalities is occurring. Hypometabolic therapy may prevent further damage and tide the brain over a critical period of perfusion–metabolism mismatch. Hypothermia to 30°C does not mask neurologic status, whereas barbiturates and other sedatives will when used in high doses.

**Increased Intravascular Volume**

Normally, CBV is regulated by the same mechanisms involved in CBF autoregulation. When autoregulation is defective, changes in arterial pressure can result in similar directional alterations in ICP. It is important to provide adequate sedation and avoid noxious stimuli as much as possible in patients with increased ICP. Increases in cerebral venous pressure can largely be attenuated by judicious positioning of the patient (fig. 10). Figure 12 demonstrates ICP reduction obtained by the use of muscle relaxants when controlled ventilation is already established. Presumably a decrease in cerebral venous pressure is the mechanism of this action. Smooth-muscle responses such as the pupillary reaction to light are not blocked by relaxants.

**CSF Retention**

Treatment of hydrocephalus in most instances is surgical redirection of the CSF outflow pathways. Besides osmotic agents, drugs such as acetazolamide and furosemide, which reduce CSF secretion by apparently different mechanisms, may be applied singly or in combination. Effectiveness of increased ICP due to hydrocephalus with these agents is usually transient.

**Postoperative Considerations**

The risk of hemorrhage into the operative site or the development of cerebral edema remains greatest within the first two days after the operative procedure. Upon return of the patient to the recovery room or neurointensive care unit, it is important that neurologic status be carefully documented. Usually the anesthetic level is light enough at this time that evaluation according to the protocol outlined above is possible. Unconsciousness presumed due to anesthesia is no excuse for not determining the level of neurologic function. After supratentorial operations the typical rostral-to-caudal progression of neurologic dysfunction will be evident in the event an intracranial complication arises.

Patients from whom needle biopsies of intracranial tumors are obtained without subsequent surgical decompression require close postoperative observation. Intracranial hypertension already present may be greatly exacerbated by the apparently minimal surgical procedure. Bleeding in the posterior fossa is dreaded because its first manifestation may be only a minor respiratory irregularity, which rapidly proceeds to apnea. After clipping of an intracranial aneurysm, there is little reason to limit stimuli directed at improving pulmonary toilet, whereas the presence of a large supratentorial cavity after tumor or hematoma evaluation may increase the propensity to bleeding into the operative site during vigorous nursing or respiratory care maneuvers. If possible, we limit such vigorous stimuli during the first 48 hours in the latter group of patients. Other complications to be anticipated postoperatively include seizures and pulmonary emboli.

Care of neurosurgical patients requires an encompassing perioperative approach rather than one limited to simply choosing an anesthetic agent. We now possess the ability to improve our therapeutic specificity in the peroperative management of patients with intracranial hypertension. Cooperation between neurosurgeon and anesthesiologist is necessary to provide optimal care for these patients.

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**Electrical Hazards**

**ELECTROCAUTERY AND VENTRICULAR FIBRILLATION** A 24-year-old patient underwent elective surgery to correct an asymptomatic atrial septal defect. Induction and maintenance of anesthesia (halothane–N₂O–O₂) were uneventful. During the initial phase of the operation, electrocauterization of most bleeding vessels was without complication. However, when the cautery was applied to the sternal periosteum in the cutting mode for 5–10 seconds, ventricular fibrillation ensued. This was followed by immediate resuscitation. Further application of the electrosurgical knife resulted in the same occurrence. At that point it was noted that the male ground plug was loose, and the unit was replaced. No further arrhythmia was encountered during the remainder of the operation. It was hypothesized that either 1) ventricular fibrillation resulted from the application of the cutting current directly to the sternum, or 2) the electrosurgical unit was at a different potential from the remaining electrical appliances in contact with the patient, resulting in fibrillation. (Hungerbuhler RS, Swope JP, Reves JG: Ventricular fibrillation associated with use of electrocautery. JAMA 230:432–435, 1974.)