STATUS EPILEPTICUS

Status epilepticus (SE) is a common neurological emergency, and it carries significant morbidity and mortality. Traditionally, SE has been defined as continuous or intermittent seizures lasting for more than 30 minutes with incomplete recovery of consciousness. However, the urgency in treating this condition necessitated a more conservative definition.1 Because there is evidence that tonic-clonic seizures rarely last more than a few minutes, the traditional definition has been discounted. Similarly, animal data suggest that fixed neuronal damage and resistance to pharmacological treatment may occur after 30 minutes of continuous seizing activity. Most experts agree that a patient is in SE if seizures persist for more than 5 minutes or if the patient’s state of consciousness does not recover between seizures.

Initial Evaluation and Management

During the initial evaluation, the clinician obtains the patient’s relevant information, paying attention to details such as history of brain injury, onset of epilepsy diagnosis, use of antiepileptic drugs (AEDs), use of psychotropic drugs, and history of substance abuse, particularly alcohol. Simultaneous evaluation and management of the airway, breathing, and circulatory state are mandatory within the first 10 minutes of initial assessment. The main principle of critical care management of SE is to treat the seizures quickly and aggressively. About 80% of patients will respond to first-line AEDs if treatment is delivered within 30 minutes of onset, but less than 40% will respond if treated within 2 hours of onset.

The preferred first-line AED is lorazepam, based on its rapid onset and prolonged action (Table 1). Lorazepam is superior to diazepam in controlling seizures at the prehospital and in-hospital levels. In a study by the Veterans Affairs Status Epilepticus Cooperative Study Group,2 treatment with lorazepam resulted in a 65% success rate versus treatment with phenobarbital (58%), diazepam plus phenytoin (56%), and phenytoin (44%); the proportion of complications, including respiratory depression, was not different among the 4 groups at 30 days. In a landmark randomized controlled clinical trial,3 respiratory depression was less associated with benzodiazepine use in the management of SE. In the Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) study, intramuscular midazolam was found to be at least as effective as IV lorazepam in prehospitalized patients with SE.

The preferred second-line agent is phenytoin or fosphenytoin (Table 1). Although no strong reason exists for this preference, this AED is the most frequently recommended second-line agent. The efficacy of phenytoin as a second-line agent has been compared with valproic acid. Several newer AEDs such as levetiracetam and lacosamide have been proposed as co-adjuvants in the management of refractory SE (RSE), but more experience is needed before a final recommendation can be made.

Third-line agents should be considered once first and second agents fail (Table 1). Intravenous midazolam is the most studied agent for the management of RSE. In a systematic review, Claassen et al4 reported that the efficacy of midazolam for the treatment of RSE was similar to that of propofol but inferior to that of pentobarbital; however, the use of midazolam was associated with more withdrawal and breakthrough seizures and fewer hemodynamic alterations. The mortality, although high, was similar in all treatment groups. Pentobarbital should be reserved for those patients failing third-line AEDs. It offers great seizure control at the expense of more complications such as hypotension, cardiac depression requiring vasopressors or inotropes, immunosuppression, and longer ICU and hospital length of stay (LOS) based on its longer half-life.

ICU Management

Those patients who meet criteria for RSE and require IV AEDs should be admitted to an ICU where continuous electroencephalography (EEG), hemodynamic...
<table>
<thead>
<tr>
<th>Stage</th>
<th>Time</th>
<th>Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resuscitation</td>
<td>0-5 min</td>
<td>Diagnosis ABCs</td>
<td>Obtain ABG, chemistry panel, blood cell counts, AED levels, toxicology tests &lt;br&gt;Order ECG &lt;br&gt;Administer thiamine, 100 mg IV &lt;br&gt;Administer Dextrose 50, 25-50 g IV, unless known glucose &lt;br&gt;Consider CT scan in comatose patients particularly if there are lateralizing signs and/or lumbar puncture, but don’t delay administration of AEDs or antibiotics.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obtain IV access Workup:</td>
<td>order EEG</td>
</tr>
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<td></td>
<td></td>
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<tr>
<td>First-line AED</td>
<td>6-10 min</td>
<td>Lorazepam</td>
<td>Dose: 0.05-0.1 mg/kg over 1-2 min, repeat in 5 min &lt;br&gt;Onset: 3-10 min &lt;br&gt;Effect: 12-24 h &lt;br&gt;Half-life: 14 h &lt;br&gt;Side effects: sedation, respiratory depression (but no different than IV phenytoin), hypotension, hyperosmolar metabolic acidosis with repetitive use secondary to accumulation of propylene glycol. Each milliliter of lorazepam injection (2 mg of lorazepam per milliliter) contains 0.8 mL of propylene glycol. Dose: 0.2 mg/kg IM up to maximum of 10 mg &lt;br&gt;Onset: 2-3 min &lt;br&gt;Effect: 2-4 h &lt;br&gt;Half-life: 2 h &lt;br&gt;Side effects: respiratory depression, hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Midazolam (IM)</td>
<td></td>
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<td></td>
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<tr>
<td>Second-line AED</td>
<td>11-20 min</td>
<td>PHT or F-PHT</td>
<td>Dose: 20 mg/kg. Rate 150 mg/min (F-PHT), or 25-50 mg/min for PHT to avoid hypotension &lt;br&gt;Onset: 20-25 min &lt;br&gt;Effect: 6-8 h &lt;br&gt;Half-life: 6 h &lt;br&gt;Side effects: 5 to 10% of patients receiving F-PHT have hypotension, arrhythmias, respiratory depression, encephalopathy, nystagmus, ataxia, hepatotoxicity, pancytopenia, Stevens-Johnson’s syndrome, hypocalcemia (F-PHT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valproic acid (Some experts consider this AED a third-line agent, but data suggest that it may be more effective than phenytoin.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alternatives</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levetiracetam</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbital</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Lacosamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dose: 30-50 mg/kg. Rate 10 mg/min &lt;br&gt;Onset: 20-25 min &lt;br&gt;Effect: 6-8 h &lt;br&gt;Half-life: 6 h &lt;br&gt;Side effects: respiratory depression, hepatotoxicity, thrombocytopenia</td>
</tr>
</tbody>
</table>
monitoring, and neurological assessments can be performed hourly. Most neurologists will direct IV AED therapy to a pattern of burst suppression, although directing the therapy to simpler seizure suppression may be an alternative for those intensivists with less experience in EEG monitoring. The two strategies, seizure suppression versus EEG burst suppression, were compared in a small study that showed no meaningful difference in outcomes. The study suggested that the lack of demonstrable advantage of treatment to burst suppression argues against the routine use of such an aggressive treatment. Additional options for the advanced management of RSE are listed in Table 2.

### Table 2. Alternatives for the Management of Refractory Status Epilepticus

<table>
<thead>
<tr>
<th>Antiepileptic drugs</th>
<th>IV levetiracetam</th>
<th>Ketamine drip</th>
<th>IV lacosamide</th>
<th>Lorazepam drip</th>
<th>Thiopental</th>
<th>Oral topiramate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthetics</td>
<td>Inhaled isoflurane</td>
<td>Lidocaine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous medications</td>
<td>Verapamil</td>
<td>Acetazolamide</td>
<td>Paraldehyde</td>
<td>Steroids</td>
<td>Corticotropin</td>
<td>IV immunoglobulin</td>
</tr>
<tr>
<td>Others</td>
<td>Ketogenic diet</td>
<td>Vagus nerve stimulation</td>
<td>Electroconvulsive therapy</td>
<td>Deep brain stimulation</td>
<td>Transcranial magnetic stimulation</td>
<td>Mild induced hypothermia (33°C-35°C; 91.4°F-95°F)</td>
</tr>
</tbody>
</table>

Information taken from references 12-17.

### ISCHEMIC STROKE

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality in the United States. In 2015, the American Heart Association (AHA) estimated that there were 610,000 new stroke cases, 185,000 recurrent strokes, and 5,700,000 stroke survivors in the United States, many requiring long-term healthcare; in the same year, at least 150,147 deaths were attributed to stroke.
Initial Evaluation and Critical Care Management

The initial evaluation and subsequent ICU management of patients with AIS are based on 5 components: (1) diagnosis; (2) thrombolysis, recanalization, and reperfusion; (3) prevention of infarct expansion, recurrence, and hemorrhagic conversion; (4) prevention and treatment of malignant cerebral edema; and (5) prevention and management of medical and neurological complications.

Diagnosis

The diagnosis of AIS is made by clinical factors, computed tomography (CT), and magnetic resonance imaging (MRI). Initial neurological evaluation and calculation of the National Institutes of Health Stroke Scale (NIHSS) (Table 3) allow for estimation of stroke burden and potential neurological outcome and for objective patient follow-up in the ICU. A noncontrast CT of the brain helps to rule out intracranial mass lesions and hemorrhages. MRI is used in some centers as part of early diagnostic and management algorithms in AIS. The use of telem medicine has the potential to improve the accuracy in diagnosis of AIS.

Thrombolysis and Recanalization

After 1995, the treatment of AIS was revolutionized by the results of the National Institutes of Neurological Disorders and Stroke (NINDS) trial. Intravenous recombinant tissue plasminogen activator (r-tPA) was initially approved in the United States for use in eligible patients within 3 hours of AIS onset. The recent results of the European Cooperative Acute Stroke Study (ECASS-III) trial confirmed the safety and efficacy of IV r-tPA in AIS patients within 4.5 hours of onset. Recent clinical trials have demonstrated that endovascular reperfusion of acutely occluded large cerebral arteries through mechanical thrombolysis improves mortality and functional outcome in eligible AIS patients. The maximal time window for successful clinical recovery after reperfusion is within 6 to 8 hours for middle cerebral artery (MCA) or internal carotid artery (ICA) occlusions and possibly 12 to 24 hours for basilar artery occlusions.

Prevention of Infarct Expansion, Recurrence, or Hemorrhagic Conversion

This phase is achieved by tight blood pressure control, temperature regulation, glycemic control, and secondary stroke prevention. Studies have reported a U-shaped relationship where poor outcome was associated with especially low and especially high admission blood pressure levels. Current guidelines from the AHA and the American Stroke Association recommend withholding antihypertensive therapy for AIS unless there is planned thrombolysis (treat to keep systolic blood pressure [SBP] <180 mm Hg or diastolic blood pressure <105 mm Hg), there is evidence of concomitant noncerebral hypertensive organ damage (eg, acute myocardial ischemia, aortic dissection, pulmonary edema, or renal failure), or the blood pressure is excessively high (SBP >220 or diastolic blood pressure >120 mm Hg), cutoffs that have been arbitrarily determined based on the upper limit of normal cerebral autoregulation.

Hemorrhagic transformation is seen in up to 9% of AIS patients. This devastating complication should be suspected in deteriorating patients with large territorial infarction, cardioembolism, systemic anticoagulation, recent thrombolytic therapy, or uncontrolled hypertension. After administration of IV r-tPA, risk factors for hemorrhagic conversion include a large area of infarction, older age, hypoglycemia, uncontrolled hypertension, congestive heart failure, and prior treatment with aspirin.

Prevention and Treatment of Malignant Cerebral Edema

MCA infarction is associated with higher morbidity and mortality compared to other infarcts. MCA strokes with an NIHSS score of less than 20, thrombus at the carotid terminus location, presence of nausea and vomiting, elevated white blood cell count, early involvement of more than 50% of the MCA territory on CT scans, and additional involvement of the anterior cerebral artery territory and/or posterior cerebral artery territory may be associated with worse edema and intracranial hypertension (Figure 1). Management of
<table>
<thead>
<tr>
<th>NIH Stroke Scale Item</th>
<th>Scoring Definitions</th>
<th>Score</th>
</tr>
</thead>
</table>
| 1a. LOC               | 0 = alert and responsive  
1 = arousable to minor stimulation  
2 = arousable only to painful stimulation  
3 = reflex responses orunarousable |       |
| 1b. LOC Questions—Ask pt’s age and month. Must be exact. | 0 = Both correct  
1 = One correct (or dysarthria, intubated, foreign lang)  
2 = Neither correct |       |
| 1c. Commands—open/close eyes, grip and release non-paretic hand, (Other 1-step commands or mimic ok) | 0 = Both correct (ok if impaired by weakness)  
1 = One correct  
2 = Neither correct |       |
| 2. Best Gaze—Horizontal EOM by voluntary or Doll’s. | 0 = Normal  
1 = partial gaze palsy; abnl gaze in 1 or both eyes  
2 = Forced eye deviation or total paresis which cannot be overcome by Doll’s. |       |
| 3. Visual Field—Use visual threat if nec. If monocular, score field of good eye. | 0 = No visual loss  
1 = Partial hemianopia, quadrantanopia, extinction  
2 = Complete hemianopia  
3 = Bilateral hemianopia or blindness |       |
| 4. Facial Palsy—If stuporous, check symmetry of grimace to pain. | 0 = Normal  
1 = minor paralysis, flat NLF, asymm smile  
2 = partial paralysis (lower face = UMN)  
3 = complete paralysis (upper & lower face) |       |
| 5. Motor Arm—arms outstretched 90 deg (sitting) or 45 deg (supine) for 10 secs. Encourage best effort. Circle paretic arm in score box | 0 = No drift × 10 secs  
1 = Drift but doesn’t hit bed  
2 = Some antigravity effort, but can’t sustain  
3 = No antigravity effort, but even minimal mvt counts  
4 = No movement at all  
X = unable to assess due to amputation, fusion, fx, etc. | L or R |
| 6. Motor Leg—raise leg to 30 deg supine × 5 secs. | 0 = No drift × 5 secs  
1 = Drift but doesn’t hit bed  
2 = Some antigravity effort, but can’t sustain  
3 = No antigravity effort, but even minimal mvt counts  
4 = No movement at all  
X = unable to assess due to amputation, fusion, fx, etc. | L or R |
| 7. Limb Ataxia—check finger-nose-finger; heel-shin; and score only if out of proportion to paralysis | 0 = No ataxia (or aphasic, hemiplegic)  
1 = ataxia in upper or lower extremity  
2 = ataxia in upper AND lower extremity  
X = unable to assess due to amputation, fusion, fx, etc. | L or R |
| 8. Sensory—Use safety pin. Check grimace or withdrawal if stuporous. Score only stroke-related losses. | 0 = Normal  
1 = mild-mod unilateral loss but pt aware of touch (or aphasic, confused)  
2 = Total loss, pt unaware of touch. Coma, bilateral loss |       |
| 9. Best Language—Describe cookie jar picture, name objects, read sentences. May use repeating, writing, stereognosis | 0 = Normal  
1 = mild-mod aphasia; (diff but partly comprehensible)  
2 = severe aphasia; (almost no info exchanged)  
3 = mute, global aphasia, coma. No 1 step commands |       |
| 10. Dysarthria—read list of words | 0 = Normal  
1 = mild-mod; slurred but intelligible  
2 = severe; unintelligible or mute  
X = intubation or mech barrier |       |
| 11. Extinction/Neglect—simultaneously touch patient on both hands, show fingers in both vis fields, ask about deficit, left hand. | 0 = Normal, none detected. (vis loss alone)  
1 = Neglects or extinguishes to double simult stimulation in any modality (vis, aud, sens, spatial, body parts)  
2 = profound neglect in more than one modality |       |

Table 4. Stepwise Approach for Management of Intracranial Pressure

| CSF drainage | Initial CSF drainage may be a lifesaving procedure, particularly in the setting of hydrocephalus and IVH. This technique allows for rapid clearance of CSF, release of ICP, and ICP/CPP monitoring. As a general rule, an ICP monitor or EVD should be placed in all comatose patients (Glasgow Coma Scale score <8) with the goal of maintaining ICP <20 mm Hg and CPP >70 mm Hg, unless their condition is so dismal that aggressive ICU care is not warranted. Compared with parenchymal monitors, EVDs carry the therapeutic advantage of allowing CSF drainage and the disadvantage of a substantial risk of infection (approximately 10% during the first 10 days). |
| Sedation | Sedation should be used to minimize pain and agitation and decrease surges in the ICP. Agitation must be avoided, because it can aggravate ICP elevation through straining (increasing thoracic, jugular venous, and systemic blood pressure), increase CMRO₂, and cause uncontrolled hyperventilation or hypoventilation, both of which can be detrimental. During an ICP spike, sedation may be all that is necessary to control the ICP. The goal of sedation should be a calm, comfortable, and cooperative state in patients with ICP that is well controlled, and a quiet, motionless state in patients in whom ICP elevation requires active management. The preferred regimen is the combination of a short-acting opioid such as fentanyl (1-3 μg/kg/h) or remifentanil (0.03-0.25 μg/kg/min) to provide analgesia, and propofol (0.3-3 mg/kg/h) because of its extremely short half-life, which makes it ideal for periodic interruption for neurological assessments; this regimen should be performed daily unless the patient’s ICP is too unstable (frequent ICP crisis in the setting of awakening, position changes, fever) to tolerate this. Bolus injections of opioids should be used with caution in patients with elevated ICP because these agents can transiently lower MAP and increase ICP due to autoregulatory vasodilation of cerebral vessels. In one trial, propofol (compared with an opioid-based sedation regimen) was associated with lower ICP and fewer ICP interventions in patients with severe traumatic brain injury. However, propofol has been associated with mitochondrial dysfunction and multiple-organ failure (propofol infusion syndrome). Predisposing factors include young age, severe critical illness of central nervous system or respiratory origin, exogenous catecholamine or glucocorticoid administration, inadequate carbohydrate intake, and subclinical mitochondrial disease. |
| CPP optimization | Two prevailing strategies for the management of elevated ICP have evolved from the experience in traumatic brain injury. The Lund concept assumes a disruption of the BBB and recommends manipulations to decrease the hydrostatic BP and increase osmotic pressures in order to minimize cerebral blood volume and vasogenic edema by improving perfusion and oxygenation to the injured areas of the brain. This is achieved in theory by maintaining a euvoletic state with normal hemoglobin, hematocrit, and plasma protein concentrations and by antagonizing vasoconstriction through reduction of catecholamine concentration in plasma and sympathetic outflow. These therapeutic measures attempt to normalize all essential hemodynamic parameters (blood pressure, plasma oncotic pressure, plasma and erythrocyte volumes, PaO₂, and PaCO₂). The introduction of microdialysis with novel physiological targets may optimize the goals of the original Lund protocol. The Rosner concept emphasizes maintaining a high CPP to minimize reflex vasodilatation or ischemia at the expense of added cardiopulmonary stress. Computerized bedside graphic displays (eg, the ICU Pilot, CMA Microdialysis, Solna, Sweden) can allow clinicians to identify whether ICP and MAP are positively correlated, in which case a low CPP would be preferable, or negatively correlated, in which case a higher CPP would be desirable. |

cerebral edema and elevated intracranial pressure (ICP) follows the same principles described in Table 4 for other neurological emergencies. Analgesia, sedation, mechanical ventilation, and hyperventilation should be used to transiently achieve a PaCO₂ of 30 to 35 mm Hg, and hyperosmolar therapy with 20% mannitol or 23.4% saline should be administered. Surgery may offer additional survival benefit to refractory cases of elevated ICP and mass effect.
Decompressive Hemicraniectomy

Four prospective randomized trials investigating the efficacy of decompressive hemicraniectomy (DHC) have been reported. DHC and durotomy more than doubled the chances of survival, from 29% to 78%. This staggering absolute risk reduction of 49% translates into a number needed to treat 2 to avoid 1 fatal outcome. The mortality reduction that results from hemicraniectomy does not come at the cost of an increased risk of survival with severe disability (ie, bedbound and completely dependent). The recently completed Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery II (DESTINY-II) clinical trial demonstrated

Hyperosmolar therapy

Hyperosmolar therapy should be used after sedation and CPP optimization fail to normalize ICP. The initial dose of mannitol is 1-1.5 g/kg of a 20% solution, followed by bolus doses of 0.25-1.0 g/kg as needed to a target osmolality of 300-320 mOsm/kg. Additional doses can be given as frequently as once an hour, based on the initial response to therapy with the anticipation of a transient decrease in BP. There is little evidence to recommend the use of standing mannitol in patients with normal ICP. Hypertonic saline, such as 23.4% saline solution, can be used as an alternative to mannitol, particularly when CPP augmentation is desirable. However, care should be taken to avoid fluid overload in the setting of heart or kidney failure. The osmotic reflection coefficient of the brain capillaries to sodium is 1.0 compared with 0.9 in the case of mannitol, indicating that HS does not effectively cross the brain capillaries, and over the first few hours of a bolus of HS, the concentration of sodium in the CSF does not change; this forms the basis of efficacy of HS as an osmotic agent effective in brain edema. Additional side effects of hyperosmolar therapy include kidney failure, rebound ICP, electrolytic imbalance (hyponatremia and hypernatremia), and acid-base disturbances. Despite clinical and animal model support, many issues remain to be clarified, including the exact mechanism of action, the best mode and timing of administration, and the most appropriate concentration.

Hyperventilation

Forced hyperventilation is generally used sparingly in the ICU and for brief periods in monitored patients, because its effect on ICP tends to last for only a few hours. Good long-term outcomes can occur when the combination of osmotherapy and hyperventilation is successfully used to reverse transtentorial herniation. Overly aggressive hyperventilation to Pco2 levels <25 mm Hg may cause excessive vasoconstriction and exacerbation of ischemia during the acute phase of ICH and should be avoided. Controlled hyperventilation therapy can be optimized by SjVO2 and PbtO2 monitoring.

Barbiturate coma

For cases of severe and intractable intracranial hypertension, barbiturates can control ICP by decreasing cerebral metabolic activity, which translates into a reduction of the CBF and cerebral blood volume. Pentobarbital can be given in repeated 5 mg/kg boluses every 15-30 min until ICP is controlled (usually 10-20 mg/kg is required) and then continuously infused at 1-4 mg/kg/h. An EEG should be continuously recorded and the pentobarbital titrated to produce a burst-suppression pattern, with approximately 6- to 8-second interbursts, to avoid excessive sedation.

Hypothermia

If pentobarbital fails to control ICP, induced hypothermia to 32°C-34°C (89.6°F-93.2°F) can effectively lower otherwise refractory ICP. Hypothermia can be achieved using various surface and endovascular cooling systems coupled to a rectal, esophageal, pulmonary artery, or bladder thermometer. Complications of hypothermia include nosocomial infection, hypotension, cardiac arrhythmias, coagulopathy, shivering, hyperkalemia, hyperglycemia, and ileus. Because these risks increase with the depth and duration of cooling, some advocate for the induction of mild hypothermia (34°C-36°C; 93.2°F-96.8°F) if temperature reduction is required for a prolonged period of time to control ICP.

**Table 4. (Continued)**

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**Abbreviations:** BBB, blood-brain barrier; BP, blood pressure; CMRO2, cerebral metabolic rate of oxygen; CPP, cerebral perfusion pressure; CSF, cerebrospinal fluid; EEG, electroencephalogram; EVD, external ventricular drain; HS, hypertonic saline; ICP, intracranial pressure; IVH, intraventricular hemorrhage; MAP, mean arterial pressure; PbtO2, brain tissue oxygen tension; SjVO2, jugular venous oxygen saturation.

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the mortality benefit offered by DHC in patients older than 60 years. In this group age, DHC does not offer a functional or neuroprotective outcome benefit as seen in younger patients (ie, <60 years).

**Deep Venous Thrombosis Prophylaxis**

Dynamic compression stockings should be placed on admission. After craniotomy, low-dose subcutaneous heparin (5,000 U, 2 or 3 times per day) starting after the second day significantly reduces the frequency of venous thromboembolism, with no increase in intracranial bleeding. Treatment with prophylaxis-dose low-molecular-weight heparin (ie, enoxaparin 40 mg daily) is a reasonable alternative.

**Nutrition**

As is the case with all critically ill neurological patients, enteral feeding should be started within 48 hours to counteract protein catabolism and malnutrition. A small-bore nasoduodenal feeding tube may reduce the risk of aspiration events. Patients who cannot take food and fluids orally should receive nasogastric, nasoduodenal, or percutaneous endoscopic gastrostomy tube feedings to maintain hydration and nutrition while undergoing efforts to restore swallowing.

**Seizure Prophylaxis**

The reported frequency of seizures during the first days of stroke ranges from 2% to 23%, but the true risk of seizures appears to be toward the lower end of this range. Seizures are more likely to occur within 24 hours of stroke and are usually partial, with or without secondary generalization. Recurrent seizures develop in 2% to 33% of patients, the rate of late seizures ranges from 3% to 67%, and SE is uncommon. The prophylactic administration of AEDs after stroke is not supported by robust data, so the treatment of seizures after AIS is based on the established management strategies for any neurological illness.

**SUBARACHNOID HEMORRHAGE**

Subarachnoid hemorrhage (SAH) from spontaneous rupture of cerebral aneurysms is the cause of 5% to 10% of strokes annually in the United States (Figure 2). Epidemiological studies suggest that the incidence rates of SAH vary substantially worldwide, with the highest rates seen in Japan and Finland. Ruptured berry aneurysms of the base of the brain are the cause of SAH in up to 85% of patients. A so-called benign pattern known as nonaneurysmal perimesencephalic hemorrhage or pretruncal SAH is seen in up to 10% of
SAHs, whereas the remaining 5% are caused by various rare conditions (Table 5). The mortality after SAH has historically been high, ranging from 30% to 70%, with 10% to 20% of these patients experiencing severe long-term neurological disability; much of this effect is related to the direct effects of hemorrhage and aneurysm rebleeding. The outcome after SAH depends on several factors, including patient age, the severity of the ictus, medical management strategies, and the development of medical complications.

Initial Evaluation and Management

The management of SAH patients should follow a consistent chronology, with an early phase aimed at stabilizing the cardiopulmonary systems, preventing early rebleeding, and managing hydrocephalus and ICP. This initial phase is followed by a period of vasospasm, during which patients require ICU care and monitoring to prevent delayed cerebral ischemia (DCI) and infarction, and a final subacute period, during which medical or neurological complications of SAH may occur. Comatose, stuporous, or lethargic patients require urgent neurosurgical evaluation for placement of an external ventricular drain. Intravenous fluids and oxygen are administered, and the standard measures of resuscitation need to be deployed: volume resuscitation, maintenance of cerebral perfusion pressure (calculated as mean arterial pressure [MAP] – ICP), blood pressure control, seizure prophylaxis, and pain and agitation control. Seizures at the onset of SAH should be aggressively treated and controlled. Patients with the diagnosis of aneurysmal SAH must be cared for in a high-volume, comprehensive center with neurosurgical and endovascular expertise. In the setting of suspected or elevated ICP, a stepwise approach should be implemented by use of analgesia, sedation, and advanced techniques (Table 4).

Targeting Early Rebleeding Risk

The initial goal of SAH care is to limit the risk of rebleeding by blood pressure control, optimization of coagulation parameters or antifibrinolytic therapy, and early aneurysm repair. Most centers actively control elevated blood pressure to a goal SBP of 140 mm Hg or less prior to open surgical or endovascular treatment of the ruptured aneurysm. Extremes of blood pressure on admission (MAP >130 or <70 mm Hg) have also been associated with poor outcome after SAH, so recognition and targeting of early blood pressure derangements may be associated with improved survival. Definitive treatment of the aneurysm is the best anti-rebleeding strategy. Early endovascular treatment and surgical treatment of ruptured aneurysms are acceptable alternatives.

Cerebral Vasospasm

Cerebral vasospasm (cVSP) is a serious medical complication that develops in at least 50% of survivors of SAH (Figure 3). With the onset of cVSP, insufficient cerebral blood flow (CBF) reaches affected regions of the brain, causing cerebral ischemia and even stroke (DCI), which could happen in 20% to 30% of patients. Although the cause of cVSP is unknown, neuroinflammatory and vasoconstricting substances originating from blood cell destruction are thought to initiate the process.

The diagnosis of cVSP may be suspected on the basis of changes in the daily neurological examination and variations of transcranial Doppler results, with cerebral angiography serving as the gold standard for its diagnosis. Most often, cVSP begins on day 3 after SAH and reaches its peak on days 6 to 8 after ictus. The symptoms are related to the vascular region of
cerebral ischemia, and if cVSP is severe enough and remains untreated, cerebral infarction may occur. Aside from its effect on mortality, one of the most important aspects of cVSP is its refractoriness to established medical interventions, emphasizing the need for additional research into the pathophysiological process of SAH-induced cerebrovascular dysfunction.

Risk factors for cVSP are related to the amount of blood seen on admission CT scans. Thick subarachnoid clot on admission CT has been associated with the development of cVSP and DCI after SAH. The Fisher CT grading scale, which evaluates the amount of cisternal blood and the presence of intraventricular hemorrhage (IVH) or intracerebral hemorrhage (ICH), is widely used to identify patients at high risk for the development of cVSP and DCI (Table 6).

**Treatment of Cerebral Vasospasm**

Medical treatment in the neurological ICU (NICU) is instituted in all SAH patients and includes intensive hemodynamic support, nutritional support, and prevention of fever, hyperglycemia, and medical complications. Maintenance of normovolemia is key in the initial management of SAH patients. The prophylactic use of the so-called triple-H therapy (hypervolemia, hypertension, hemodilution) is not recommended anymore because the only technique consistently shown to improve CBF is induced hypertension.

Nimodipine is the most widely administered agent after SAH based on its relative selectivity for dilation of the

Figure 3. Cerebral vasospasm after subarachnoid hemorrhage
cerebral arteries compared with the systemic vasculature. Although nimodipine does not appear to decrease angiographic vasospasm, multiple trials have shown that this agent improves outcomes by decreasing the incidence of cerebral ischemia. Angioplasty and intra-arterial vasodilators, either alone or in combination, are the mainstay of therapy for vasospasm after SAH.

Medical and Neurological Complications

Medical complications of SAH are summarized in Table 7. These include cardiac arrhythmias and ventricular dysfunction, fever, seizures, hyperglycemia, nosocomial infections (sepsis, pneumonia, ventiliculitis, meningitis, among others), and a host of other intrinsic or iatrogenic medical complications such as anemia, elevated ICP, hydrocephalus with shunt dependency, and electrolyte imbalances. Of these complications, rebleeding, DCI, fever, anemia, and hyperglycemia are associated with worse neurological outcomes.

INTRACEREBRAL HEMORRHAGE

Nontraumatic forms of ICH account for 10% to 30% of all hospital admissions for stroke (Figure 4). Death at 1 year varies by location of the lesion: 51% for deep, 57% for lobar, 42% for cerebellar, and 65% for brain stem hemorrhages. In approximately 40% of cases, blood may extend into the ventricles (IVH), substantially worsening the prognosis and potentially leading to neurological death related to acute obstructive hydrocephalus.

Table 6. Risk of Vasospasm According to Fisher and Modified Fisher Grading Systems

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Risk of Vasospasm (Symptomatic), %</th>
<th>Grade</th>
<th>Definition</th>
<th>Risk of Vasospasm (Symptomatic), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No blood</td>
<td>21</td>
<td>0</td>
<td>No SAH or IVH</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Thin blood</td>
<td>25</td>
<td>1</td>
<td>Minimal/thin SAH, no IVH in both ventricles</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>Thick blood</td>
<td>37</td>
<td>2</td>
<td>Minimal/thin SAH, with IVH in both ventricles</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>Predominantly ICH or IVH</td>
<td>31</td>
<td>3</td>
<td>Thick SAH, no IVH in both ventricles</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>Thick SAH, with IVH in both ventricles</td>
<td>40</td>
</tr>
</tbody>
</table>

Abbreviations: ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; SAH, subarachnoid hemorrhage.


Initial Evaluation and Management

Medical therapies for ICH are limited to guidelines or expert opinions regarding blood pressure reduction, ICP monitoring, osmotherapy with fluid resuscitation, fever and

Table 7. Medical and Neurological Complications After Subarachnoid Hemorrhage

<table>
<thead>
<tr>
<th>Medical complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (temperature &gt;38.3°C or &gt;100.94°F)</td>
</tr>
<tr>
<td>Anemia (hemoglobin &lt;9 mg/dL)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Hypermagnesemia</td>
</tr>
<tr>
<td>Hyponatremia</td>
</tr>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
</tr>
<tr>
<td>Bloodstream infection</td>
</tr>
<tr>
<td>Urinary tract infections</td>
</tr>
<tr>
<td>Cardiac</td>
</tr>
<tr>
<td>Hypotension requiring vasopressors and inotropes</td>
</tr>
<tr>
<td>Arrhythmias</td>
</tr>
<tr>
<td>High cardiac troponin</td>
</tr>
<tr>
<td>Decreased left ventricular ejection fraction</td>
</tr>
<tr>
<td>Pulmonary</td>
</tr>
<tr>
<td>Pulmonary edema</td>
</tr>
<tr>
<td>Neurological complications</td>
</tr>
<tr>
<td>Seizures</td>
</tr>
<tr>
<td>Late hydrocephalus, shunt dependency</td>
</tr>
</tbody>
</table>

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glycemic control, and care in a specialized stroke unit or NICU. Recently published guidelines for the management of spontaneous ICH in adults provide helpful, evidence-based recommendations.

**Diagnosis**

Noncontrast CT scan of the brain is the method of choice to evaluate the presence of ICH. CT scan evaluates the size and location of the hematoma, extension into the ventricular system, degree of surrounding edema, and anatomic disruption. Hematoma volume may be easily calculated from CT scan images by use of the ABC2 method, a formula derived from the calculation of the volume of the sphere.

Conventional diagnostic cerebral angiography should be reserved for patients in whom secondary causes of ICH are suspected, such as aneurysms, arteriovenous malformations, cortical vein or dural sinus thrombosis, or vasculitis. Findings on CT scan or MRI that should prompt angiographic study include the presence of SAH, IVH, underlying calcification, or lobar hemorrhage in nonhypertensive younger patients. The role of angiography after ICH has been addressed by 2 studies. Zhu et al reported abnormalities on angiography in 48% of patients who were normotensive and younger than 45 years of age, 49% of patients with lobar hemorrhages, and 65% with isolated IVH; the investigators reported no abnormalities in patients older than 45 years who had a history of hypertension with subcortical ICH. Halpin et al reported finding an underlying lesion in 84% of patients who appeared to have a structural abnormality seen previously on brain imaging. Diagnostic catheter angiography should be strongly considered in all patients with primary IVH and in younger nonhypertensive patients with lobar ICH.

**Emergency Department Management**

Rapid neurological deterioration and ensuing loss of consciousness with impairment of reflexes that maintain airway protection mandate that airway control be secured. Failure to recognize imminent airway loss may result in complications such as aspiration, hypoxemia, and hypercapnia. Dextrose-containing solutions should be avoided as

![Figure 4. Spontaneous intracerebral hemorrhage]( Courtesy of Rincon and Mayer.)
Blood Pressure Control

Blood pressure is frequently elevated in patients with acute ICH, and these elevations in blood pressure are greater than those seen in patients with ischemic stroke. Potential explanations for this phenomenon include upregulation of the neuroendocrine system via the sympathetic nervous system, renin–angiotensin axis, pituitary–adrenal axis, and increased ICP. The presence or degree of acute hypertension may affect the outcome after ICH. Single-center studies and a systematic review have reported an increased risk of deterioration, death, or dependency with increased admission blood pressure after ICH.

Several clinical trials have evaluated the role of intensive blood pressure reduction after ICH. The phase III clinical trial INTERACT-II (Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial) concluded that intensive lowering of blood pressure did not result in a significant reduction in the rate of the primary outcome of death or severe disability. However, a trend was observed when the primary outcome was analyzed in an ordinal fashion, suggesting that in a selected cohort of ICH patients, intensive lowering of blood pressure may improve long-term outcomes. The Antihypertensive Treatment in Acute Cerebral Haemorrhage (ATACH) trial also confirmed the feasibility and safety of early, rapid blood pressure reduction in ICH without benefit in long-term functional outcome. Both INTERACT and ATACH have shown that while early and intensive blood pressure lowering is clinically feasible and safe, this does not affect clinical outcomes.

Guidelines from the AHA indicate that when SBP exceeds 200 mm Hg or MAP exceeds 150 mm Hg after ICH, management of blood pressure should be achieved with continuous infusion of antihypertensive agents. For those patients with SBP higher than 180 mm Hg or MAP higher than 130 mm Hg and with the possibility of elevated ICP, ICP monitoring should be considered and blood pressure should be lowered using intermittent or continuous IV medications, while maintaining a cerebral perfusion pressure greater than 60 mm Hg. If no elevated ICP is suspected, then targeting a modest reduction of blood pressure is reasonable. In the setting of impaired CBF auto-regulation, excessive blood pressure reduction may exacerbate ischemia in the area surrounding the hematoma and worsen perihematomal brain injury. The AHA has recommended that for patients with SBP of 150 to 220 mm Hg, lowering SBP to 140 mm Hg is probably safe.

Preferred agents are β-blockers and calcium channel blockers. Use of nitroprusside has drawbacks, since this agent is associated with a higher rate of medical complications and may exacerbate cerebral edema and ICP. Oral and sublingual agents are not recommended because of the need for immediate and precise blood pressure control. Although no prospective study has addressed the timing of conversion from IV to oral antihypertensive management, this process can generally be started between 24 and 72 hours, as long as the patient’s critical condition has been stabilized.

Initial Emergency ICP Management

Emergency measures for ICP control are appropriate for stuporous or comatose patients or those who present acutely with clinical signs of brainstem herniation (ie, pupillary abnormalities or motor posturing). The patient’s head should be elevated to 30°, 1.0 to 1.5 g/kg of 20% mannitol should be administered by a rapid infusion, and the patient should be hyperventilated to a PaCO₂ of 26 to 30 mm Hg. As a second-line therapy, or if the patient is relatively hypotensive, 0.5 to 2.0 mL/kg of 23.4% saline solution can be administered through a central venous line. These measures are 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. Corticosteroids are contraindicated based on the results of randomized trials that have failed to demonstrate efficacy in ICH. Neurosurgical consultation is warranted for those patients with rapidly declining mental status and hydrocephalus with IVH seen in the initial CT scan. Early placement of a ventricular drain in this case may be lifesaving (Table 4).

Hemostatic Therapy

Hematoma size is an important determinant of mortality after ICH, and early hematoma growth, defined as an increase in hematoma size within 6 hours after onset, is consistently associated with poorer clinical outcomes and an increased mortality rate. Similarly, significantly greater reductions in Glasgow Coma Scale and NIHSS scores have been reported among patients with documented hematoma growth on 1-hour follow-up CT scans versus those without growth.

In the phase III Efficacy and Safety of Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage (FAST) clinical trial, 80- and 20-μg/kg doses of recombinant activated factor VII were compared against placebo in an...
overall trial population of 841 ICH patients. No significant difference was found in the main outcome measure, which was the proportion of patients with death or severe disability according to the modified Rankin scale at 90 days (Table 8) (score of 5 or 6), but the hemostatic effect and side effect profiles were confirmed. A preliminary clinical study of the antifibrinolytic agent ε-aminocaproic acid was conducted with negative results. The Management of ICH With Aminocaproic Acid open-label pilot study (MANICHAN-PILOT) and the Antifibrinolytic Therapy in Acute Intracerebral Hemorrhage (ATICH) clinical trial have also been designed to test the hypothesis that ε-aminocaproic acid administration within 3 hours of ICH is associated with less hematoma growth and improved outcomes.

**Reversal of Anticoagulation**

Anticoagulation with warfarin increases the risk of ICH by 5- to 10-fold in the general population, and approximately 15% of ICH cases overall are associated with the use of this agent. Patients with ICH receiving warfarin should be reversed immediately with fresh frozen plasma (FFP) or prothrombin complex concentrate and vitamin K (Table 9). Prothrombin complex concentrate contains vitamin K–dependent coagulation factors II, VII, IX, and X; normalizes the international normalized ratio (INR) more rapidly than does FFP; and can be given in smaller volumes but carries a higher risk for development of disseminated intravascular coagulation. In the INR Normalization in Coumadin

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms at all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>


Patients with ICH who have been anticoagulated with unfractionated or low-molecular-weight heparin should be reversed with protamine sulfate, and patients with thrombocytopenia or platelet dysfunction can be treated with a single dose of desmopressin, platelet transfusions, or both (Table 9). In patients with abnormal platelet assays and risk of poorer outcome, early platelet transfusion improved platelet activity assay results and was associated with smaller final hemorrhage size and more independence at 3 months. The recently finished Platelet Transfusion in Cerebral Hemorrhage (PATCH) clinical trial demonstrated that platelet transfusion did not improve the risk of hematoma growth and was associated with worse functional outcome in ICH patients who were receiving antplatelet treatment.

Newer agents such as direct thrombin inhibitors and factor Xa inhibitors provide a new challenge for the reversal of coagulopathy-related ICH. A newly approved antidote is available for the direct thrombin inhibitor dabigatran (Table 9). In patients with a strong indication for anticoagulation, such as a mechanical heart valve or atrial fibrillation with a history of cardioembolic stroke, anticoagulation can be safely restarted after 10 days.

**ICU Management**

Observation in an ICU or a similar setting is strongly recommended for at least the first 24 hours after ictus, since the risk of neurological deterioration is highest during this period and because the majority of patients with brainstem or cerebellar hemorrhage have depressed level of consciousness, requiring ventilatory support. Measurements in the ICU that are indicated for the optimal cardiovascular monitoring of ICH patients include invasive arterial blood pressure, central venous pressure, and, under rare circumstances, pulmonary artery catheter monitoring. An external ventricular drain should be placed in patients with depressed level of consciousness, signs of acute hydrocephalus or intracranial mass effect on CT, and a prognosis that warrants aggressive ICU care.

**Patient Positioning**

To minimize ICP and reduce the risk of ventilator-associated pneumonia in mechanically ventilated patients, the patient’s head should be elevated 30°.
Fluids

Isotonic fluids such as 0.9% saline at a rate of approximately 1 mL/kg/h should be given as the standard IV replacement fluid for patients with ICH and should be optimized to achieve euvolemic balance and an hourly urine output of greater than 0.5 mL/kg. Free water given in the form of 0.45% saline or 5% dextrose in water can exacerbate cerebral edema and increase ICP because the water flows down its osmotic gradient into injured brain tissue. Systemic hyposmolality (<280 mOsm/L) should be aggressively treated with mannitol or 3% hypertonic saline. The use of hypertonic saline in the form of a 2% or 3% sodium chloride–acetate solution (1 mL/kg/h) has become an increasingly popular alternative to normal saline as a resuscitation fluid for patients with significant perihematoma edema and mass effect after ICH. The goal is to establish and maintain a baseline state of hyperosmolality (300-320 mOsm/L) and hypernatremia (150-155 mEq/L), which may reduce cellular swelling and decrease the number of ICP crises. Potential complications of hypertonic saline use are fluid overload, pulmonary edema, hypokalemia, cardiac arrhythmias, hyperchloremic metabolic acidosis, and dilutional coagulopathy. Hypertonic saline should be gradually tapered and the serum sodium level should never be allowed to drop more than 12 mEq/L over 24 hours, to avoid rebound cerebral edema and recurrence of increased ICP.

Table 9. Emergency Management of the Coagulopathic Patient With Intracerebral Hemorrhage

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Agent</th>
<th>Dose</th>
<th>Level of Evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Fresh frozen plasma or 3- or 4-factor PCC</td>
<td>10-15 mL/kg</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>and Vitamin K</td>
<td>15-30 U/kg</td>
<td>II</td>
</tr>
<tr>
<td>Direct thrombin inhibitor</td>
<td>Dabigatran</td>
<td>10 mg IV</td>
<td>II</td>
</tr>
<tr>
<td>Direct factor Xa inhibitors</td>
<td>Activated charcoal within 2 h of ingestion</td>
<td>50 g IV (in 2 vials each containing 2.5 g/50 mL)</td>
<td>I</td>
</tr>
<tr>
<td>(apixaban, edoxaban, rivaroxaban)</td>
<td>Idarucizumab</td>
<td></td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>Consider hemodialysis or idarucizumab redosing for refractory bleeding after initial administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other direct thrombin inhibitors</td>
<td>Activated PCC (FEIBA) or 4-factor PCC</td>
<td>50 U/kg IV</td>
<td>II</td>
</tr>
<tr>
<td>Abbreviations: FEIBA, factor eight inhibitor bypassing activity; PCC, prothrombin complex concentrate.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Class I, based on 1 or more high-quality randomized controlled trials; class II, based on 2 or more high-quality prospective or retrospective cohort studies; class III, case reports and series, expert opinion.

Reprinted from *The Lancet Neurology*, 4, Mayer SA, Rincon F, Treatment of intracerebral haemorrhage, 662-672, Copyright (2005), with permission from Elsevier.
Surgical Intervention for ICH

Craniotomy has been the most studied intervention for the surgical management of ICH, but the results have been discouraging. The Surgical Trial in Intracerebral Haemorrhage (STICH), a landmark trial of more than 1,000 ICH patients, showed that emergent surgical hematoma evacuation via craniotomy within 72 hours of onset failed to improve outcome compared with a strategy of initial medical management. In contrast to supratentorial ICH, there is much better evidence that cerebellar hemorrhages exceeding 3 cm in diameter benefit from emergent surgical evacuation, given that abrupt and dramatic deterioration to coma can occur within the first 24 hours of onset in these patients. For this reason, it is generally unwise to defer surgery in these patients until further clinical deterioration occurs.

Because emergent craniotomy has been unable to improve neurological outcome after ICH, the role of other surgical techniques such as minimally invasive surgery has gained importance over the last decade. The advantages of minimally invasive surgery over conventional craniotomy include reduced operative time, the possibility of performance under local anesthesia, and reduced surgical trauma. A recent preliminary analysis of data from the Minimally Invasive Surgery Plus rtPA for Intracerebral Hemorrhage Evacuation (MISTIE) study revealed that the technique was associated with significant reductions in perihematomal edema, cost benefits, and improved outcomes at 1 year.

Hemicraniectomy with duraplasty has been proposed as a lifesaving intervention for several neurological catastrophes such as large hemispheric infarct (LHI) and poor-grade SAH. No randomized controlled trial of this intervention has been conducted in patients with ICH. In a recent report of 12 consecutive patients with hypertensive ICH who were treated with hemicraniectomy, 11 (92%) survived at discharge and 6 of them (54.5%) had a good functional outcome (modified Rankin Scale, 0-3). Another case-control study suggested that patients with ICH associated with significant cerebral edema and an ICH score greater than 2 may potentially benefit from DHC.

Deep Venous Thrombosis Prophylaxis

Like patients with AIS, patients with ICH are at high risk for venous thromboembolism, a potentially fatal complication, due to limb paresis and prolonged immobilization. Prophylaxis strategies are the same as described above for patients with AIS.
NEUROGENIC RESPIRATORY FAILURE

Neuromuscular disorders (NMDs) leading to weakness and mixed respiratory failure may be encountered by the intensivist in the emergency department or ICU. The most important NMDs are myasthenia gravis (MG) with exacerbations or crisis, cholinergic crisis in MG patients, acute inflammatory demyelinating or axonal neuropathies (Guillain–Barre syndrome [GBS], with all variants including the Miller–Fisher variant), Lambert–Eaton myasthenic syndrome, botulism, tick paralysis, organophosphate intoxication, N–hexane (glue sniffing) intoxication, fish poisoning (ciguatera, tetrodotoxin, saxitoxin), myopathies (polymyositis–dermatomyositis, acid maltase deficiency, critical illness myopathy or neuropathy, undiagnosed mitochondrial myopathies, among others), and magnesium overdoses, particularly in the management of critically ill pregnant women and neurocritical care patients (magnesium may be used as an antishivering agent). In people not vaccinated for diphtheria/pertussis/tetanus or polio, the intensivist might encounter diphtheria or polio-induced neuropathy or neuropathy.

Initial Evaluation and Management

Establishing a history is important to arrive at a syndromic, anatomic, and possibly etiological diagnosis. Determining whether the patient is really weak or fatigued, malnourished, or just unwilling to cooperate is an important part of the initial evaluation. History of prior crisis or admissions to the hospital is relevant for patients with MG or Lambert–Eaton myasthenic syndrome. Exposure to specific foods, diarrhea or viral illnesses, travel to tick endemic areas, and history of recent vaccinations are important for patients with GBS, tick diseases, or fish poisoning. Absence of vaccination for diphtheria/pertussis/tetanus in particular social groups or residents from abroad who develop upper respiratory tract infections is relevant for the diagnosis of diphtheria or polio. A family history of NMDs is important to establish the diagnosis of certain autosomal dominant or recessive myopathies, neuropathies, and mitochondrial diseases. Particular odors, psychiatric history, or specific findings during the initial evaluation, such as hypersalivation or urinary retention, may help establishing a diagnosis of organophosphate intoxication. Similarly, history of therapeutic high–dose magnesium exposure in an areflexic patient is indicative of magnesium toxicity. Finally, patients with prolonged ICU LOS who are exposed to uncontrolled hyperglycemia, neuromuscular paralysis, gram-negative sepsis, and aminoglycosides, among others, may be at risk for critical illness myopathy or neuropathy.

Initial laboratory studies should include complete blood cell counts, chemistry panel, liver function tests, creatine kinase levels, chest radiograph, electrocardiograph, arterial blood gases, and lumbar puncture for evaluation of cerebrospinal fluid (in case of suspected GBS). Additional urgent testing, based on results of a thorough neurological evaluation, such as brain or spinal cord imaging with CT or MRI, may be important to rule out life–threatening conditions such as basilar thrombosis, brainstem ICH/AIS, and spinal cord compression. Electromyography and nerve conduction studies, although important, have a low yield during the acute setting for most of the NMDs, so these tests may not be considered urgent in these circumstances.

ICU Management

Patients with suspected acute NMDs, acute on chronic exacerbations of NMDs, or crisis of NMDs should be admitted to an ICU or to an intermediate care or telemetry unit, where vital signs and neurological status can be assessed frequently. The initial assessment of ventilatory function is very important. Patients with NMDs should undergo urgent assessment of respiratory function at the bedside. Vital capacity and the negative inspiratory force may be assessed by a respiratory therapist and should be reassessed frequently. Ventilatory assistance may be required or preferred in those patients with vital capacity less than 15 mL/kg or negative inspiratory forces less than 20 cm H2O. The arterial blood gases, although informative, are usually unreliable because most patients become acutely hypercarbic or hypoxic only after overt respiratory failure has occurred. Noninvasive intermittent positive pressure ventilation is the most efficient method of increasing alveolar ventilation without intubation.

Myasthenic Specific Treatments

MG is a relatively rare autoimmune disorder of the peripheral nerves in which antibodies form against acetylcholine nicotinic postsynaptic receptors at the neuromuscular junction. A reduction in the number of acetylcholine receptors induces progressively reduced muscle strength with repeated use of the muscles and reduced recovery of muscle strength following a period of rest. The bulbar or axial muscles are affected most commonly and most severely, but most patients also develop some degree of fluctuating general weakness. Myasthenic crisis is characterized by severe axial muscle weakness, abnormalities in the vital signs, and progression to respiratory failure. Cholinergic crisis is also seen and is the result of exaggerated cholinergic activity, usually induced by overdose of anticholinesterase inhibitors (pyridostigmine) and characterized by bradycardia, urinary retention, and increased oral secretions. In early myasthenic crisis, pyridostigmine is typically held since it can aggravate secretions, and underlying precipitants should
be addressed and treated accordingly. Rapid treatment with IV immunoglobulin (IVIG) or plasmapheresis is indicated, with both having comparable efficacy, but IVIG may be preferred in patients with hemodynamic compromise, in whom plasmapheresis may be contraindicated. Steroids may be given concomitantly, but intensivists should expect an exacerbation in muscle weakness within 5 to 10 days after initiation of this therapy in about 50% of patients, of whom 10% will then require mechanical ventilation. The steroid-induced exacerbation tapers off very quickly (within 5–7 days) and may be attenuated by concomitant avoidance therapy (IVIG, plasmapheresis). The anticholinesterase inhibitors may be restarted once the patient has improved clinically. Mortality after MG crisis is relatively low (<5%), but the mean duration of mechanical ventilation may be up to 2 weeks. Predictors of prolonged mechanical ventilation and prolonged ICU and hospital LOS include initial HCO₃ greater than 30 mEq/dL, peak vital capacity on days 1 to 6 postintubation less than 25 mL/kg, and older age (>50 years).

Specific Treatments for Guillain-Barre Syndrome

GBS consists of a rare group of immune-mediated polyneuropathies characterized by motor, sensory, and autonomic dysfunction. GBS is the most frequent cause for subacute flaccid, areflexic paralysis in the United States (1–3 per 100,000 people). The origin of GBS is related to molecular mimicry triggered by certain infections and activation of the T-cell–mediated response against ganglioside molecules in the surface of peripheral nerves. Clinical suspicion is raised by the onset of subacute ascending and areflexic paralysis characterized by albumin-cytological dissociation in the cerebrospinal fluid. Similar to MG crisis, GBS requires surveillance of ventilatory function. Treatment with plasma exchange and IVIG has been studied in clinical trials, and these treatments enhance recovery with similar efficacy; corticosteroids are not beneficial. Prognosis is usually good; mortality is lower than 5%, and up to 90% of patients experience full recovery within 6 to 12 months. Predictors of poor outcome include older age, rapid onset, preceding diarrheal disease, respiratory failure, and axonal variants.

Specific Treatments for Critical Illness Polyneuropathy and Critical Illness Myopathy (CIP/CIM)

Critically ill patients are at risk of developing severe weakness secondary to CIP/CIM. The incidence of CIP/CIM in these patients has been estimated to be around 33% to 44%. The incidence may be higher in septic patients, those exposed to neuromuscular blocking agents, those who have used steroids, and those with hyperglycemia. The mortality of CIP/CIM has been reported between 26% and 71%; up to 70% of patients may recover after 6 months, but 30% may have long-term sequelae. Specific therapies to treat this condition are lacking, but it may be prevented or attenuated by avoiding use of neuromuscular blocking agents, avoiding prolonged use of steroids, and initiating early physical therapy. In one study, tight glycemic control was associated with lower incidence of CIP and fewer ventilator weaning days, suggesting that hyperglycemia may play a role in the pathophysiological process of CIP.

REFERENCES


SUGGESTED READING


