Resource-Limited ENLS
Intracranial Hypertension and Herniation

Diagnosis and management of intracranial hypertension in resource-limited settings follows the principles developed for ICP management in high-income settings, but is likely to be constrained by resource gaps that affect multiple domains of care. These include pre-hospital care, timely diagnostic neuroimaging, access to ICP-lowering pharmacotherapy, and capacity for ventriculostomy and invasive ICP monitoring.

Pre-hospital care and patient transport: Because of worldwide underdevelopment of pre-hospital systems of care, patients with intracranial hypertension in resource-limited settings are likely to be brought to medical attention by family members or community bystanders, and to present with undifferentiated coma. Patients presenting to low-resource health facilities should be transferred to the highest feasible level of care, ideally a referral center equipped with a CT scanner and an intensive care unit (ICU), and staffed with neurological, neurosurgical, and critical care expertise. The safety and risks of transporting patients with evidence of intracranial hypertension must be weighed by the triaging clinician on an individual basis, accounting for the patient's clinical stability after assessing circulation, airway, and breathing, as well as the travel distance and means of transport to a referral center. If possible, the airway should be secured before transport, though many resource-limited facilities lack this capability. If an ambulance is unavailable, care should be taken to elevate the patient's head during transport either by placing pillows or other supports under the head and shoulders or placing the patient in a partially reclined car seat. Patients with concern for unstable spine fracture should be positioned flat and immobilized as able. Midline head position should be maintained with a rigid cervical collar if available, or by placing sandbags or pillows on either side of the patient's head. While the risk of secondary brain injury is high during transport, this risk must be weighed in the context of the initial center's resource limitations, the available interventions at the referral center, and a recognition that the natural history of untreated intracranial hypertension is likely to result in poor outcomes or death if transfer is not pursued.

***Initial evaluation*:** While some resource-limited centers may have the capacity to organize emergent CT imaging in the emergency department, many facilities experience prolonged delays to obtaining CT because of high inpatient scanner demand, scanner down times, and the need for patients to furnish out-of-pocket funds before imaging. When urgent neuroimaging is unavailable, clinicians must rely on a detailed clinical history and neurologic exam to assess for intracranial hypertension as a possible cause of altered mental status. After stabilization of the patient's circulation, airway, and breathing, and cervical spine, the Glasgow Coma Scale (GCS) score should be determined, and a targeted neurologic exam should be performed to assess for clinical signs of increased ICP. These include decreased level of consciousness, asymmetric or non-reactive pupils, unilateral or bilateral abducens palsies, fixed downward gaze, vomiting, Cushing's physiology, posturing, or papilledema on funduscopic examination.

Tiered ICP-lowering therapies: Tier 0 therapies in resource-limited settings are similar to those indicated in high-income settings. Hospital beds in many resource-limited facilities lack a mechanism for raising the head of bed, in which case the head of the mattress can be propped up with rolled blankets or boxes to maintain at least 30 degrees of elevation. Timely measurement of the serum sodium may be delayed depending on turnaround times from the clinical laboratory, and lack of access to hypertonic saline may limit therapeutic options for correcting hyponatremia. In the absence of hypertonic saline, hyponatremia correction may be pursued with a 1L/day free water restriction and administration of salt tablets if available via nasogastric tube.

Available tier 1 therapies are likely to be limited in most under-resourced settings, although mannitol is available in most tertiary care facilities in low- and middle-income countries and is on the World Health Organization's List of Essential Medicines. Patients who continue to show clinical signs of intracranial hypertension despite tier 0 therapies should be treated with mannitol 0.5-1g/kg and/or hypertonic saline, though the latter is largely unavailable outside of high-income settings. The safety of mannitol administration must be considered in the context of available laboratory monitoring for serum osmolarity, osmolar gap, and renal function. These parameters should ideally be monitored daily for patients on intermittent therapy and every 6 hours for patients on standing therapy, though depending on laboratory capacity, available monitoring may be less frequent. Care should be taken to monitor the patient's volume status and replace urinary losses with isotonic fluids. Lasix should be avoided as an ICP-lowering therapy but may be considered if other indications for diuresis exist. Similarly, availability of arterial blood gas sampling or end tidal CO2 monitoring may dictate the feasibility and safety of temporary hyperventilation. In the absence of blood gas monitoring, an empiric respiratory rate of 20 while escalating to higher tier therapies is likely safe. Patients with evidence of acute hydrocephalus should undergo CSF diversion with an external ventricular drain (EVD) if ventriculostomy catheter is available and can be placed safely. Most resource-limited settings lack capacity for quantitative ICP monitoring, and clinicians should follow institutional protocols to determine goals and clinical endpoints for CSF drainage. Lumbar puncture should be avoided until CT is performed to assess structural risk of downward herniation, including space-occupying lesions displacing midline structures, cerebral edema, obstructive hydrocephalus, or effacement of the basal cisterns. If EVD is unavailable and CT discloses no contraindication to lumbar puncture, CSF diversion may be achieved via lumbar drain if available, or via serial lumbar puncture.

Tier 2 therapies in resource-limited settings are similar to those in high-resource settings. Available hyperosmolar therapies should be maximized and administered on a standing basis unless serum monitoring indicates a serum osmolar gap >20mOsm/kg for mannitol or a serum sodium >160mEq/L for hypertonic saline (if available). Propofol and midazolam infusions are available in most resource-limited tertiary care settings for reduction of cerebral metabolic demand and blood volume. Because deep sedation limits bedside monitoring of the neurologic exam, and because invasive ICP monitoring is unavailable in most resource-limited settings, serial CT imaging should be considered for sedated patients as access allows. Frequent lifting of sedation for patients with acute brain injury increases cerebral metabolic demand and should be limited in patients receiving tier 2 therapies. Depending on the patient's clinical status, a daily examination off sedation with all consulting staff present may be reasonable, with hourly pupil exams in the interim.

Tier 3 therapies are likely to limited to rescue surgical interventions in centers with neurosurgical capability. Pentobarbital is not widely available in low- and middle-income countries. Therapeutic hypothermia may be considered through the use of ice packs or chilled saline, though medications and interventions to limit shivering, a driver of secondary brain injury, are likely to be limited.

Context-specific protocols: Access to ICP-lowering therapies varies widely among resource-limited healthcare settings, and protocols for ICP management must reflect individual institutions' diagnostic and therapeutic resource availability. The CREVICE protocol[1], adapted from the non-invasive monitoring strategy employed in the BEST-TRIP trial[2], provides an example of how ICP management may be protocolized in a resource-limited setting (Figure 1), and may serve as a starting point for that specialists can use to develop protocols that reflect the existing capacities at individual institutions.

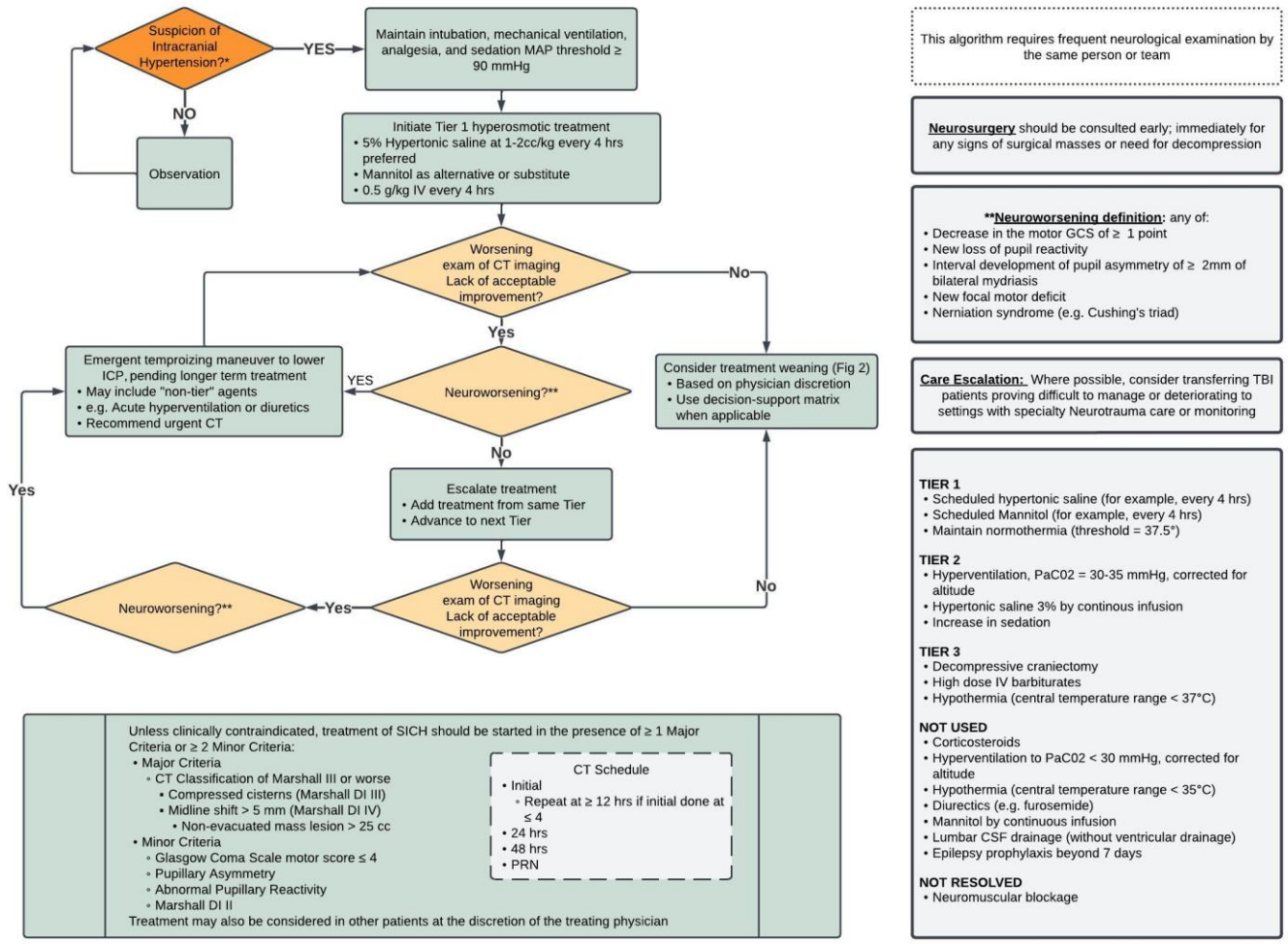

Figure 1

CREVICE protocol for clinical neuromonitoring in settings without invasive ICP monitoring (from Chesnut et al., *J Neurotrauma* 2020)

References

1. Chesnut RM, Temkin N, Videtta W, Petroni G, Lujan S, Pridgeon J, Dikmen S, Chaddock K, Barber J, MacHamer J, Guadagnoli N, Hendrickson P, Aguilera S, Alanis V, Bello Quezada ME, et al. Consensus-Based Management Protocol (CREVICE Protocol) for the Treatment of Severe Traumatic Brain Injury Based on Imaging and Clinical Examination for Use When Intracranial Pressure Monitoring Is Not Employed. *Journal of neurotrauma*. 2020;37(11):1291–1299.

2. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, Petroni G, Lujan S, Pridgeon J, Barber J, Machamer J, Chaddock K, Celix JM, Cherner M, Hendrix T. A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury. *New England Journal of Medicine*. 2012;367(26):2471–2481.