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Management of the Pediatric Neurocritical Care Patient

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Introduction

When Peter Safar established the multidisciplinary, critical care training program at the University of Pittsburgh in the 1960's, he did so as part of a lifelong goal to save "...the person with a heart and brain too good to die."¹ In the ensuing decades, the field of critical care medicine has bloomed into a robust specialty that has largely followed Dr. Safar's prescient vision. For modern clinicians charged with the care of critically-ill children, the protection and restoration of neurologic function involves increasingly sophisticated management strategies and technologies that have been rapidly changing in recent decades.

Brain injury is commonly encountered in pediatric critical care and has been attributed to 65% of all deaths in the pediatric intensive care unit (PICU).² Traumatic brain injury (TBI) is the leading cause of death and disability of children, though patients with an admission diagnosis of TBI make up only 14% of pediatric neurocritical illness.^{3–5} The causes of critical brain injury in childhood are diverse, stemming from a number of medical and surgical diseases (Table 1). The gravity of preserving the developing brain's neurologic potential in the face of complex, heterogeneous pathophysiologies has fostered the sub-field of pediatric neurocritical care.

This review aims to introduce the reader to the specialty of pediatric neurocritical care (PNCC) while highlighting established management practices, recent breakthroughs and ongoing controversies in the field. A comprehensive discussion of any single disease is beyond the scope of this article. Instead, the historic context of modern pediatric neurocritical care models is reviewed, followed by an overview of contemporary monitoring strategies and brief discussion of the major disease categories encountered in PNCC. Finally, we conclude with potential that PNCC holds for the future of children's health.

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Pediatric Neurocritical Care as a Service

Though neurointensive care is often viewed as a newer sub-field of critical care, the specialty's roots can be traced back for quite some time. In 1932, Dr. W. E. Dandy developed a post-operative neurosurgical unit for patients at the Johns Hopkins Hospital⁶ and the poliomyelitis epidemics of the late 1940's and 1950's led to a surge in hospitals in Europe and North America opening critical care units for this disease that attacks the ventral horn cells of the spinal cord.⁷ Critical care units for adults with a myriad of neurological conditions – neurotrauma, neurovascular, neuromuscular and others – became commonplace over time. Ultimately, the United Council for Neurologic Subspecialties administered the first certification examination for Neurocritical Care in 2006.

In 1955, the first PICU opened at Children's Hospital of Goteburg in Sweden⁸, followed by similar units in the US over the next decade or more. Most recently, specialized PNCC services evolved in several locations with varying personnel and goals. In the early 2000s, Boston Children's Hospital developed a model of PNCC consisting of consulting neurologists providing critical-care specific expertise in the acute phase of care and follow-up on hospital wards.^{8,9} An alternative model was developed at Children's National Medical Center (Washington, DC) consisting of a pediatric intensivist, neurologist and several neurosurgeons serving as a cohesive team for all neurosurgical and neurological admissions to the PICU, as well as children suffering from new neurological injuries.³ Other variations of the PNCC model sprouted in the 2000's, with services emerging at other tertiary centers, including Lurie Children's Hospital (dedicated neurologists/intensivists in a 4-person team who consult on all PNCC patients), St. Louis Children's Hospital (protocol-based care for children with severe traumatic brain injury) and Children's Hospital of Pittsburgh (intensivist-led team who provides primary care for children with neurological/neurosurgical conditions).^{3,10,11}

Currently, outcomes and deliverables remain understudied in the field. In the consult model developed at Children's National Medical Center, the PNCC service was responsible for adding diagnostic considerations to the differential in 40% of consults.³ At St. Louis Children's Hospital, establishment of a PNCC service was associated with a reduction in TBI-associated death from 11% to 3% and an increase in favorable disposition from 33% to 67% - though some limitations of the study include that some of the more severely injured subject were excluded from the analysis.¹¹ The impact of dedicated PNCC services appears promising, though much work remains in determining how such models influence outcomes.

Neuromonitoring

Preventing secondary injury is a central tenet of modern neurocritical care, with insults such as hypotension, hyperthermia, hypoxia, hypoglycemia, intracranial hypertension and seizures believed to potentiate initial brain injuries and contribute to an unfavorable outcomes.^{12–15} While conventional intensive care monitoring largely focuses on cardiorespiratory parameters^{16–21}, a variety of brain-specific monitoring strategies and techniques have been used in children. Such neuromonitoring systems include scores derived from physical examinations, imaging modalities, electroencephalography (EEG) tracings,

intracranial pressure (ICP) measurements and brain oxygenation information. All have played some role in monitoring the neurologically-injured child with varying degrees of applicability.

Physical Examination

The most ubiquitous, standardized approach to assessing, following and conveying a neurologically injured patient's condition is the Glasgow Coma Scale (GCS). The GCS ranges from 3 to 15, representing an aggregate of the eye, verbal and motor scores. A modified scale exists for infants and small children.^{22,23} GCS scores after traumatic brain injury have been positively correlated with outcomes^{24–26}, yet the score alone provides imperfect discrimination of injury severity and prognosis in the middle of its range.^{25,27–31} It also remains largely un-validated outside of trauma and does not correlate well with airway protective reflexes.^{32–34} In a move to address limitations inherent to the application of the GCS to patients in the ICU, alternative systems such as the Full Outline of Unresponsiveness (FOUR) score have been developed, yet have performed comparably but not superior to the GCS in outcome prediction.^{35,36}

Imaging

Physical exam and GCS thresholds play a significant role in the decision to pursue neuroimaging. The utility of computed tomography (CT) imaging to detect neurological emergencies is still a primary tool of clinicians in contemporary practice, yet there has been concern raised in recent years surrounding the risk of acquired malignancies.^{37–39} Current estimates indicate an incidence of 1 new malignancy case for every 1,000 to 10,000 CT scans in children younger than 15 years of age^{40,41}, with dose attenuation protocols aimed at minimizing these risks becoming common.^{42–45} While the decisions for “routine” CT scans likely needs to be reconsidered, the use of CT scans for diagnosing neurological emergencies remains an important part of clinical practice.

Adjuvant use of non-radiating imaging modalities have begun to be incorporated into practice. Fast sequence or rapid magnetic resonance imaging can be used to evaluate and follow hydrocephalus and requires shorter scanning times compared to traditional MRI.^{46,47} Rapid MRI has been explored for acute trauma imaging with good correlation with CT for parenchymal and extra-axial lesions, though CT remains superior for fracture detection.^{47,48} MRI susceptibility weighted imaging (SWI) and fluid attenuation inversion recovery (FLAIR) modes are superior for the detection of small traumatic hemorrhages and edema, respectively, relative to CT.^{49,50} Transcranial Doppler (TCD) has also been studied across a range of critical brain injury, with particular utility in assessing autoregulation and vasospasm.^{51,52} In the PNCC, the use of TCD is promising but continues to depend on center-specific experience and familiarity.

Cerebral Oximetry and Perfusion

A range of tools have been developed to evaluate cerebral oxygenation in PNCC patients. Jugular venous oximetry (SjO₂) can be used to monitor global cerebral oxygen extraction. While it has been used to guide intraoperative support, its utility within the ICU remains unclear.^{53–56} Near-infrared spectroscopy (NIRS) is a non-invasive approach to oximetry that

measures absorption of light in the near-infrared spectrum via a sensor adhered to a patient's forehead.^{57,58} In theory, the applied sensor measures oxygenation of the underlying cortex while filtering out the oxygenation of the skin and subcutaneous tissue. A major limitation of NIRS is its regional assessment that may or may not be an accurate surrogate of global cerebral oxygenation.⁵⁶ Measurement of partial pressure of brain tissue oxygen (PbO₂) can be accomplished by a commercially-available monitor inserted into the cerebral cortex. The majority of the existing literature with PbO₂ monitoring exists after TBI, with evidence suggesting that PbO₂ values <10 mmHg associated with unfavorable outcome.^{59–61} Similar to NIRS, PbO₂ monitors only a select region of tissue, but have a higher face validity than NIRS monitoring with the current technology.

Cerebral perfusion pressure is determined by the arithmetic difference between mean arterial pressure (MAP) and ICP. Monitoring ICP can be accomplished by strain-gauge devices placed within the brain parenchyma or indwelling catheters placed within the cerebral ventricle.^{62,63} Considerable controversy exists regarding when to monitor ICP and whether targeting perfusion goals or pressure goals should guide management. In patients with CNS infections, perfusion-guided management may be superior to ICP-guided therapy.⁶⁴ For trauma patients, the BEST:TRIP trial included adult TBI patients and failed to demonstrate the superiority of ICP monitoring over a protocol based on clinical examination and imaging.^{65,66} In contrast, ICP-driven therapy in TBI has been associated with lower mortality in several studies.^{67–69}

Electroencephalography (EEG)

Of children admitted to the hospital with a neurologic diagnosis, more than 50% have seizures, either as a primary diagnosis or in relation to a number of other neurologic diagnoses.^{70,71} EEG remains the gold standard for diagnosing seizures. Clinical seizures are normally readily identifiable, yet should be confirmed with EEG in most instances. Subclinical seizures require EEG analysis for detection and the use of anti-epileptic medications in this instance is controversial. After TBI, seizures occur in approximately 12% in the first 7 days following injury, with risk factors including severity of injury, young age, and abusive head trauma.^{15,72,73} Approximately one third of patients with seizures following TBI experience subclinical status epilepticus, with younger age, abusive trauma, and intraaxial bleed representing risk factors in one series.⁷⁴ Subclinical seizures have been identified in almost 7% of neonates after cardiac surgery and in 18% of pediatric patients with any acute encephalopathy^{75,76}, with early electrographic seizures associated with development of epilepsy and adverse outcomes.^{74,76,77}

Continuous EEG (cEEG) – defined as continuously obtaining and interpreting EEG data over hours or longer – has become a standard monitoring approach for patients at high-risk for subclinical seizures.⁷⁸ While cEEG generates data that can be analyzed in real-time, a survey of PICUs determined the most common practice is for physicians to formally review CEEG twice daily.⁷⁸ Amplitude-integrated EEG (a-EEG) and density or compressed spectral array (DCSA) are approaches that compress several hours of EEG data in a graphical interface meant to be more readily interpretable by bedside clinicians and nurses.⁷⁷ a-EEG has become commonplace in neonatology, however both a-EEG and DCSA have highly

variable sensitivities for detecting seizure activity in the PICU and are not yet routinely used.⁷⁹

CNS Emergencies

Many management approaches are subject to controversies stemming from the paucity of randomized controlled trials in PNCC; however, several common themes have emerged in recent years across all categories of brain injury. The importance of preventing inadvertent hyponatremia has been recognized and frequent assessment with active management of hyponatremia stemming from either cerebral salt wasting or the syndrome of inappropriate antidiuretic hormone has become a cornerstone of care.^{80,81} Likewise, while the best application of hypothermia remains unclear, aggressive prevention of hyperthermia is now standard practice when managing brain injury across a range of etiologies.¹⁰² Both hyponatremia and hyperthermia join a number of other factors in lowering seizure threshold in the setting of CNS disease. Routine surveillance with EEG and seizure prophylaxis has become more common in recent years, though the optimal application of these interventions is unclear.^{77,82}

Most interventions aimed at mitigating irreversible brain damage are time-dependent and management strategies can be broadly categorized according to the primary injury process. The most commonly encountered CNS emergencies in PNCC are (i) disorders of intracranial hypertension (increased ICP) and compromised cerebral perfusion, (ii) seizures and status epilepticus, (iii) cerebral ischemia from embolic and thrombotic stroke, (iv) infectious and non-infectious CNS inflammation and (v) hypoxic injury. Considerable overlap exists in the pathophysiologic mechanisms underlying these brain injuries of different etiologies, with a complex interplay between excitotoxic pathways, cascades of inflammatory and apoptotic responses, propagation of free radical species, and mitochondrial dysfunction contributing to clinical outcome.^{83–85}

Intracranial Hypertension

Intracranial hypertension can stem from any number of injury processes and generally follows the basic principle outlined within the Monro-Kellie doctrine. Within this framework, the intracranial pressure is derived from the volume of the intracranial contents (including brain tissue, cerebrospinal fluid [CSF], arterial/venous blood volumes and pathological fluid collections) and the fixed-volume of the relatively rigid cranium. Compensatory mechanisms – such as displacement of CSF into the lumbar spinal column – can ameliorate alterations in cerebral volume to a point. After those have been overcome, increases in cerebral volume lead inexorably to increases in intracranial pressure. Left unchecked, these processes lead to cerebral herniation.⁸⁶

Considerable debate exists regarding treatment thresholds for ICP to avoid negative consequences – with many clinicians believing that ICP should be treated if it is greater than 20 mm Hg or if the patient is symptomatic. Treatments for intracranial hypertension include hyperventilation, elevating the head of the bed to 30°, maintaining the head in a midline position to promote venous drainage, administration of the osmotic agents and reducing cerebral metabolic demand with sedatives.^{87,88} Neurosurgical interventions may be

necessary, with timing of such interventions dependent upon consideration of risks and benefits. For severe TBI, evidenced-based guidelines exist to treat intracranial hypertension among other aspects of TBI care. These guidelines suggest that a threshold of ICP of 20 mm Hg may be considered⁸⁹ and outlines general considerations of treatments outlined above. Disappointingly, the only Level 2 recommendation recommending a treatment be applied – indicating a strategy that should be considered – involves the use of hypertonic saline for ICP control. Other therapies lack sufficient evidence to provide guidance to clinicians at this time.

The subtype of edema – cytotoxic from swollen brain cells or vasogenic from increased fluid in interstitial fluid - may be useful in guiding therapy. Dexamethasone is a mainstay of treatment for tumor-associated vasogenic cerebral edema.^{90,91} Glucocorticoids have also been shown to reduce hearing loss and improve neurologic outcome associated with bacterial meningitis, and to reduce mortality associated with *Streptococcus pneumonia* meningitis, working, in part, by reducing inflammation and edema in the subarachnoid space.⁹² Osmotherapy is frequently employed for cerebral edema, though disease-specific evidence is largely lacking. In DKA, a retrospective study of an administrative dataset found a higher incidence of mortality amongst children who received hypertonic saline as compared to those who received mannitol.⁹³

Surgical intervention can provide definitive therapy for some diagnoses causing intracranial hypertension. Non-communicating or obstructive hydrocephalus is relieved with CSF drainage. Malfunction of an existing ventricular shunt requires prompt recognition and urgent surgical revision. Proximal and distal catheter occlusion, disconnection and infection are the most common indications for revision.⁹⁴

Seizures and Status Epilepticus

As outlined above, seizures are a common diagnosis in the PNCC. A multicenter, retrospective review of children undergoing EEG in the ICU demonstrated that 30% had electrographic seizures and 38% of children with seizures had electrographic status epilepticus.^{95,96} Many diagnoses encountered in critically-ill children are associated with seizures, including TBI, CNS infections, neuromalignancy, ischemic and hemorrhagic stroke, extracorporeal life support (ECLS), epilepsy, complex febrile seizures, hypoxic-ischemic encephalopathy, and autoinflammatory disease.^{71,97} Early recognition of seizures is crucial, as prolonged treatment initiation is associated with increased therapy refractoriness, a phenomenon potentially related to time-dependent changes in GABA receptors.^{98–100} Electrographic status epilepticus has been independently associated with a higher risk for mortality amongst critically-ill children.^{95,101} Notably, one retrospective case series suggested that 24% of seizure-related deaths are preventable.¹⁰² A separate retrospective cohort study demonstrated that children admitted to the ICU with status epilepticus were less likely to have been managed according to a therapy protocol compared to children who were admitted to the acute care ward, 26% versus 66%.¹⁰³ Identifying high-risk patients can guide the use of continuous EEG, a resource-intense monitoring strategy that may be cost-effective if its use helps to improve outcomes by as little as 3% for 24-hours of monitoring.¹⁰⁴

Standardization of treatment of status epilepticus has been incorporated into guidelines by the Neurocritical Care Society. These guidelines¹⁰⁰ recommend an appropriately-dosed benzodiazepine as a first-line agent after a Cochrane review found that lorazepam was more effective than placebo, diazepam and phenytoin in seizure cessation.¹⁰⁵ A subsequent prospective, randomized, controlled trial studied a total of 273 children who received either lorazepam or diazepam for the treatment of status epilepticus failed to demonstrate significant differences in clinically-important outcomes, however.¹⁰⁶ Treatment of status epilepticus – seizures lasting for > 5 minutes without cessation – has also been included in the guidelines. After initial therapy with benzodiazepines, second-line treatments for status epilepticus include phenytoin or fosphenytoin and phenobarbital, with the latter preferred for infants.¹⁰⁰ Phenytoin and its derivatives can worsen seizures in children with Dravet syndrome and should be avoided, as the disease is caused by a mutation in the SCN1A sodium channel, a phenytoin target.¹⁰⁷ Propofol is generally avoided for the treatment status epilepticus in children given the risks of propofol-related infusion syndrome.⁹⁹ Levetiracetam has also been reported to be effective in the management of status epilepticus in children, though no randomized controlled trial has been performed.^{108–110} Future work is necessary to clarify subtypes of status epilepticus in children amenable to tailored antiepileptic therapy.

Ischemic Stroke

Acute ischemic stroke (AIS) is significantly less common than either TBI or seizures in children, with an estimated incidence of 1–2 cases per 100,000 per year.^{111,112} The risk of AIS in children is age-related, with younger age conferring higher risk. There are approximately 4 cases of AIS per 100,000 per year in those less than 1 year of age¹¹¹ and certain co-morbidities are associated with an increased risk of AIS. A cohort study of all children admitted with cancer at a single tertiary center over 9 years demonstrated that 5 patients in a cohort of 1,411 had suffered AIS.¹¹³ The incidence of AIS in children with sickle cell disease is also considerably higher than the general population, with approximately 235 cases per 100,000 per year.¹¹⁴ Children who have had a previous stroke associated with a vascular abnormality detected on imaging have a 5-year recurrence rate of 66%.¹¹⁵ While such co-morbidities carry an increased risk of stroke, one retrospective case series examining new presentations of ischemic stroke in children at a tertiary emergency department found that 56% occurred in previously healthy patients.¹¹⁶

Symptomatology varies with AIS. According to one center's experience, 64% of children with AIS had focal limb weakness, 60% had facial weakness, and 46% had speech disturbances.¹¹⁶ Patients with confirmed or suspected AIS are commonly admitted to the ICU for sequential neurologic exams and consideration is given to initiation of anticoagulation strategies. It has been proposed that children with AIS may be at higher risk of elevated ICP compared to adults, as childhood strokes more often occur in larger vessels and less cerebral atrophy provides less room to accommodate edema.¹¹⁷ A retrospective review of childhood AIS over 10 years in Northern California demonstrated that 61% were admitted to the ICU, 32% were intubated and 11% underwent decompressive craniectomy.¹¹⁸ While in the ICU, hemodynamic parameters are monitored closely, with permissive hypertension often allowed in order to promote perfusion of injured nervous

tissue, a strategy derived from the management of adult AIS.¹¹⁹ Notably, a recent retrospective study of a large administrative database found an association between hypertension and in-hospital mortality in children presenting with AIS.¹²⁰

Adult AIS management emphasizes time windows during which medical thrombolysis or mechanical thrombectomy can be employed to salvage viable brain tissue, which has not been adequately studied in children.^{121,122} Contemporary management of AIS in children remains largely derived from the adult literature and guided by the experience of individual centers, as well as a number of case reports and series.^{123–126} No prospective study has yet evaluated the efficacy of either thrombolysis or thrombectomy in the pediatric population. Unfortunately, the National Institute of Neurological Disorders and Stroke funded the Thrombolysis in Pediatric Stroke (TIPS) trial was stopped due to lack of enrollment of subjects.¹²⁷ The foundation for current stroke management in children is based on supportive care and considerations of anticoagulation.

CNS Infections and Inflammation

The incidence of meningitis and encephalitis in children greater than 2 months old has decreased dramatically in the post-vaccination era.¹²⁸ Accordingly, the epidemiology of CNS infections encountered in the PNCC setting has shifted to include less previously healthy children and a greater proportion of children with significant pre-existing comorbidities, particularly at tertiary centers. Primary or secondary immunosuppression places patients at risk for both common and uncommon CNS pathogens.¹²⁹ Intracranial devices can serve as a nidus for infection, with the duration of EVD placement being directly related to the risk of infection.¹³⁰ Initial management of any CNS infection parallels the treatment of other acute infections in pediatric critical care, with concomitant early delivery of antibiotics, cardiorespiratory support and consideration of removing the nidus of infection. For the acutely ill child presenting with either focal neurologic symptoms or symptoms of shock, empiric coverage with broad-spectrum antibiotics capable of crossing the blood-brain barrier is required.¹³¹ In addition to a third-generation cephalosporin, the addition of vancomycin should be considered with the increased prevalence of resistant gram-positive bacteria. Importantly, the cellular differential of CSF pleocytosis should not be used to dissuade the clinician from empiric initial treatment of potential bacterial infections in the ill-appearing patient, as the relative predominance of neutrophils is not discriminatory between aseptic and septic CNS infections.¹³² Urgent medical intervention may be insufficient for certain processes. Intracranial abscesses and subdural empyema may require surgical drainage.^{133,134} CNS fungal infections can also progress despite appropriate antimicrobial coverage, particularly in immunosuppressed patients, and pathogens such as mucormycosis require manual debridement for effective source control.¹³⁵

Non-infectious CNS inflammatory diseases are increasingly encountered in the PNCC setting. Acute disseminated encephalomyelitis (ADEM) is classically observed 1–2 weeks after a viral infection - with presenting features of encephalopathy, including altered mental status, focal neurologic deficits and seizures.¹³⁶ The pathogenesis involves inappropriate T-cell responses that lead to CNS demyelination - corresponding to hyperintense lesions in the subcortical and central white matter on T2-weighted and fluid-attenuated inversion recovery

MRI. Anti-body mediated encephalitis is another autoimmune CNS inflammatory process that is being recognized more often in PNCC. The most widely described of these diseases is anti-N-methyl-D-aspartate receptor antibody (NMDAR) encephalitis, a paraneoplastic process frequently triggered by the emergence of an ovarian teratoma in girls under 14 years of age.¹³⁷ A recent cohort study in California surveying the frequency of infectious and noninfectious encephalitis noted that the incidence of NMDAR was four times that of West Nile Virus, Herpes Simplex Virus-1, or Varicella Zoster Virus encephalitis.¹³⁸ A number of other autoantibodies have also been identified as mediators of encephalitis in children. Case series and descriptive studies point to a subset of patients with comparable symptoms but no identifiable culprit antibody, suggestive of pathogenic antibodies that remain to be elucidated.¹³⁹ For the PNCC clinician, treatment of non-infectious CNS inflammatory disorders relies on addressing associated seizures alongside a combination of corticosteroids, intravenous immunoglobulin, and plasmapheresis for treatment refractory or particularly severe cases.¹⁴⁰ Co-management of these patients with pediatric neurologists and rheumatologists is often helpful given the lack of conclusive evidence for guiding therapies.

Post-Anoxia Brain Injury

Considerable progress has been made in recent decades to characterize the mechanisms responsible for brain cell death in response to hypoxia. Coarsely summarized, oxygen starvation triggers a cascade of cell death-related pathways leading to damage throughout the brain even after adequate oxygen supply has been restored to the brain.^{141,142} Care of the patient who has suffered cardiac arrest or isolated severe hypoxia focuses on optimizing physiologic conditions for the injured brain while preventing additional insults. The recent 2015 update to the American Heart Association (AHA) guidelines for cardiopulmonary resuscitation recommend maintaining normocapnia and normoxia following cardiac arrest, the use of fluids and vasopressors to prevent hypotension, and targeted temperature management consisting of continuous normothermia (36°C to 37.5°C) for 5 days or hypothermia (32°C to 34°C) for 2 days followed by normothermia for 3 days.¹⁴³

To investigate the utility of hypothermia, the Therapeutic Hypothermia after Out-of-Hospital Cardiac Arrest (THAPCA) trial randomized 295 children ages 2 days to 18 years who remained unconscious after out-of-hospital cardiac arrest to undergo either controlled normothermia or hypothermia for 5 days.¹⁴⁴ The primary outcome of survival with a good neurobehavioral score was met by 20% of the hypothermia group versus 12% of those in the normothermia group, $p=0.14$. At present, hypothermia remains an option for some clinicians although the utility of the maneuver is still unclear given the THAPCA findings.

The Future of Pediatric Neurocritical Care

As outlined above, the diversity of neurological disorders of critically-ill children is quite vast and the care of such children is becoming increasingly complex. Various institutions have decided to dedicate resources to developing models of PNCC delivery in an effort to standardize care and achieve improved outcomes. It is clear that these efforts must involve multiple specialties – intensivists, neurologists and neurosurgeons at a minimum – with follow-up necessary to determine the effects of the changes in clinical practice. It remains

unclear if all major institutions need to have such an approach or if dedicated teams in select institutions can generate sufficient information to change practice for the entire field. At this time, it appears that PNCC will likely play an important role in the health of children with critical neurological conditions.

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Table 1

Disorders of Pediatric Neurocritical Care

Traumatic Brain Injury (TBI)
<i>Subdural hemorrhage</i>
<i>Epidural hemorrhage</i>
<i>Cerebral contusion</i>
<i>Subarachnoid hemorrhage</i>
<i>Diffuse axonal injury</i>
<i>Penetrating TBI</i>
Seizures and Status Epilepticus
<i>Epilepsy</i>
<i>Complex febrile seizures</i>
<i>Seizures secondary to other primary CNS disease (TBI, malignancy, infection, toxidrome, etc.)</i>
Ischemic Stroke
Sinus Venous Thrombosis
Metabolic Stroke
Ruptured Arteriovenous Malformation
Infectious Encephalitis and Meningitis
<i>Bacterial infection</i>
<i>Viral infection</i>
<i>Fungal infection</i>
<i>Mycobacteria infection</i>
Autoimmune Encephalitis and Encephalomyelitis
<i>Post-infectious autoinflammation and Acute Disseminated Encephalomyelitis (ADEM)</i>
<i>Antibody-mediated autoinflammation and paraneoplastic diseases</i>
Intracranial Abscess and Empyema
Cerebral Edema Secondary to Metabolic and Endocrine Diseases
<i>Diabetic ketoacidosis</i>
<i>Disorders of ammonium production and metabolism</i>
<i>Acute, pronounced fluctuations in serum sodium</i>
<i>Mitochondrial disease</i>
Post-Hypoxic Brain Injury and Cerebral Edema
Hydrocephalus
Intracranial Neoplasms