Historical Vignettes

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Past, Present and Future of the Treatment of Traumatic Brain Injury in Children and Adolescents

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HISTORICAL BACKGROUND

The first clinical evidence of Traumatic Brain Injury (TBI) was discovered in prehistoric Tanzania, with findings dating back to approximately 2 million years BC in the pre-historic period, in Tanzania, apparently due to a crocodile bite demonstrating cranial fractures [1]. The earliest written records appear in the Edwin Smith Papyrus (Ancient Egypt, ~3000–2500 BC), which described head injuries, skull fractures, and neurological symptoms, establishing the first known classification of TBI severity. There were 27 head injury cases of which 13 were fractures with neurological involvement. The Edwin Smith Papyrus is still preserved at the New York Academy of Medicine in New York City [1,2]. The recognition that children require distinct treatment from adults is a much more recent achievement. Initially based solely on the presence or absence of skull fractures, later shifting toward the neurological deficits observed. For centuries, injured children were treated merely as "small adults," with identical therapeutic approaches and no recognition of the physiological peculiarities of the developing brain [3,4].
Historically, the lack of pediatric-specific protocols was one of the greatest challenges in caring for children with TBI. Decisions on performing CT scans or invasive intracranial pressure (ICP) monitoring were based on extrapolations from adult studies, which often led to unnecessary radiation exposure in children or, on the other hand, delayed diagnosis of intracranial lesions. Furthermore, the absence of evidence-based guidelines for the pediatric ICU meant that practices such as deep sedation, hyperventilation, and barbiturate coma therapy were used inconsistently, with significant variation among institutions and a lack of clear target parameters [4,5,6].

PRESENT

In the present, specific protocols have transformed pediatric neurotrauma care. The PECARN (Pediatric Emergency Care Applied Research Network) [7] rule represents a milestone: a rigorously validated clinical decision rule that allows clinicians to safely identify children at low risk of clinically significant TBI, avoiding unnecessary CT scans and their associated radiation. Developed from a large multicenter cohort (over 42,000 children), the PECARN rule has high sensitivity and an excellent negative predictive value, substantially reducing radiation exposure in the pediatric

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population [7]. In the ICU setting, the publication of evidence-based guidelines, such as those from the Brain Trauma Foundation [8], standardized the management of severe pediatric TBI. Current recommendations encompass multimodal neuromonitoring (ICP, brain tissue oxygenation — PbtO2, and continuous electroencephalography), strict thermal control, maintenance of adequate cerebral perfusion pressure (CPP) with age-adjusted targets, hyperosmolar therapy (mannitol), and, in selected cases, decompressive craniectomy. The recognition that the immature brain has a distinct neurometabolic cascade post-trauma including prolonged ionic flux, mitochondrial dysfunction, and increased vulnerability to excitotoxicity has also driven the development of age-appropriate neuroprotective strategies [4,5,8].

FUTURE

The future focuses on Precision Medicine, with the integration of serum and neuroimaging biomarkers aimed at personalized diagnosis and prognosis [9,10]. Biomarkers such as GFAP (Glial Fibrillary Acidic Protein), UCH-L1 (Ubiquitin C-terminal Hydrolase L1), NfL (Neurofilament Light Chain), and a panel of inflammatory cytokines are being validated to stratify lesion severity, predict outcome, and guide therapeutic decisions without relying exclusively on clinical and conventional imaging criteria. Together with advances in genomics and pharmacogenomics, the goal is to develop individualized neuroprotective drugs that modulate specific pathways — such as the neuroinflammatory cascade, oxidative stress, and apoptosis — in a manner tailored to each patient's genetic profile [3,9,10]. Artificial Intelligence (AI) — particularly Machine Learning algorithms — emerges as a transformative tool. Predictive models fed by continuous ICP, PbtO2, and multimodal hemodynamic data are being developed for real-time monitoring, capable of anticipating episodes of intracranial hypertension and cerebral hypoperfusion minutes before they occur, enabling proactive rather than merely reactive interventions [8,9].

DIFFERENCES BETWEEN THE INFANT AND ADOLESCENT BRAIN

Identifying the pathophysiological differences of TBI between infants and adolescents is essential for appropriate clinical management. At the extremes of childhood, the cranial and cerebral characteristics are profoundly distinct, directly influencing the response to trauma.

The Brain and Skull of the Infant (0 to 2 Years) [3,4,6]

- Cranial Compliance: The infant's skull has open fontanelles and non-fused sutures, providing a natural expansibility that can mask classic signs of intracranial hypertension for longer periods. Paradoxically, this same compliance makes the brain more vulnerable to contrecoup injuries and parenchymal deformation during impacts.

- Trauma Mechanics: The disproportionately large head relative to the body, combined with weak cervical musculature, predisposes infants to high-energy acceleration-deceleration injuries (angular acceleration), such as those seen in abusive head trauma (shaken baby syndrome). The immature, highly aqueous brain (with reduced myelin) undergoes greater deformation under shear stress.

- Vulnerability to Hypovolemia: The total blood volume in an infant is significantly lower in absolute terms compared to adolescents. Intracranial hemorrhage or even extensive subgaleal hematomas can rapidly lead to hypovolemic shock — a phenomenon rarely seen in older children or adults after an isolated head injury.

The Brain and Skull of the Adolescent

- Monro-Kellie Doctrine: the skull becomes a rigid, non-expandable compartment. Hence, the Monro-Kellie doctrine applies fully: the sum of intracranial volumes is constant, and any increase in one component must be compensated by the displacement of another; once compensation is exhausted, ICP rises exponentially.

- Diffuse Axonal Injury (DAI): The adolescent brain is more myelinated, creating a higher density interface between gray and white matter. Acceleration/deceleration and rotational forces promote severe diffuse axonal injury from shear forces; a mechanism strongly associated with unfavorable neurological outcomes.
- Malignant Brain Swelling: Adolescents are particularly prone to "malignant brain swelling," a phenomenon of acute hyperemia (vascular congestion) followed by diffuse cytotoxic edema, often refractory to conventional treatment. The management priority in this age group is strict ICP control through staged protocols that combine sedation, hyperosmolar therapy, moderate hyperventilation, and in extreme cases, decompressive craniectomy [7,8,10].

In summary, while in the infant the open skull offers some degree of protection against rapid increases in ICP but increases susceptibility to traumatic vascular and hypovolemic lesions, in the adolescent the rigid skull imposes the Monro-Kellie doctrine, with higher risk of diffuse axonal injury and malignant swelling that require aggressive ICP management. Understanding these differences is fundamental to tailoring care at each stage of development.

Final Remarks

The guidelines and consensus references that underpin the current management of TBI in children and adolescents are primarily derived from multicenter studies and systematic reviews, such as those by Kochanek et al. (2019) [8], the Brain Trauma Foundation pediatric guidelines, the PECARN studies led by Kuppermann et al. (2009) [7] for head CT decision rules, Giza and Hovda (2014) [5] for the neurometabolic cascade of concussion, and the recent reviews by Mayer et al. (2025) [10] and Chiollaz et al (2025) [9] on biomarkers and precision medicine in pediatric TBI.

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