Whereas other areas of medicine have entered an apparent golden era of personalized medicine, the neurotrauma field is still struggling with comparatively basic issues. The landmark work of Weed and McKibben (see Wilkins et al.) established hyperosmolar therapy as an effective treatment for intracranial hypertension a century ago. This work was disruptive because it introduced the new notion that the brain could change its volume. A century before that—long before Cajal’s work and the advent of neuron theory—the writings of Monro and Kellie espoused the belief that the volume of the brain was constant.

Despite the unquestionable and marked efficacy of this life-saving therapeutic strategy, insufficient literature has come forth over the last 100 years to inform the best use of hyperosmolar therapy. Indeed, the recently published fourth edition of the Brain Trauma Foundation (BTF) Guidelines for the Management of Severe Traumatic Brain Injury (TBI) failed to find any evidence meeting current standards on which to base recommendations. Thus, there is a tremendous need to better understand the different properties of hypertonic saline and mannitol and how these agents are best administered to the critically ill patients who require them.

Although I acknowledge the substantial deficiencies in the literature as well as opinions that differ from my own, I have been concerned with some practices related to hyperosmolar therapy that seem increasingly prevalent and that are discordant with important laboratory and clinical evidence that we do have—as well as the subspecialty training I received from leading figures in the field of neurotrauma. First, it is my impression that liberal and even prophylactic administration of hyperosmolar therapy is increasingly commonplace. In my region, first responders now frequently administer hypertonic saline to normotensive patients suspected of having intracranial pathology but who do not show signs of herniation or a progressive neurological deficit. This is despite the recommendations in the BTF’s guidelines not to do so because of the harm associated with the prophylactic treatment of intracranial pressure with hyperosmolar and other therapies.

In this regard, it is important for clinicians to be aware of laboratory investigations that have demonstrated that homeostatic mechanisms see the increased production of osmoles by the brain in hypernatremic or hyperosmolar states. These additional brain osmoles aim to maintain the volume of the brain and reduce the concentration gradient between the brain and the administered hyperosmolar therapies. This phenomenon is referred to as brain adaptation, and it has been extensively studied and described in the older literature. The volume of water that will cross a semipermeable membrane is, of course, dependent on the concentration gradient between the two compartments. On the basis of theory as well as experimental observations, there is thus concern that prophylactic administration of hyperosmolar therapy makes it less effective when its administration is truly required.

A highly related second concern that I have is the practice of sodium targeting—or trying to achieve and maintain a specific serum sodium concentration in the high normal or supranormal range in hopes of avoiding or reducing intracranial hypertension. The concern with sodium targeting is that it is at least to a certain degree prophylactic, invoking the issues described above. An additional concern is with continuous (non-bolus) hyperosmolar therapy infusions that are often prescribed as part of sodium targeting strategies. Here the issue is that the small concentration gradient generated limits the efficacy of this approach. Indeed, continuous infusion of hyperosmolar therapy for the management of intracranial pressure is a contravention of the American College of Surgeons’ Trauma Quality Improvement Program consensus statements.
promises after TBI. This new paper by Vedantam et al.
concentration of 10 g/dl or greater is similarly inadvisable
ing the cerebral perfusion pressure above 70 mm Hg is
To date, her group has demonstrated that routinely push -
ction of practitioners taking something assumed to be good
group’s important works has been the repeated demonstra
of practitioners taking something assumed to be good
have great respect for Claudia Robertson and the impact-
2017 National Neurotrauma Symposium by the AANS/
Indeed, this work was recently awarded Best Poster at the
issues, but I belong to a group of neurotraumatologists
nation, we need more high-quality research to inform these
sodium with poor outcome. This is not new.
thresholds are specific to the patient and the situation.
er harm than the intracranial pressure they aim to treat.
sodium and osmolality are associated with great
thresholds would be those at which
be safely administered. Some practitioners use a higher
of 155 mEq/L (and osmolality of 320 mOsm/L) is general
may be associated with the best outcome from TBI.
ysis of “big data” in the IMPACT study allowed the con
interpretation of the spline functions presented in that
is that a sodium level of approximately 142 mmol/L
may be associated with the best outcome from TBI.
In my opinion, the study by Vedantam et al.9 should
particularly cause us to scrutinize the sodium limits asso-
ciated with hyperosmolar therapies. A serum sodium level of
155 mEq/L (and osmolality of 320 mOsm/L) is generally
considered to be the upper limit at which mannitol can be
safety administered. Some practitioners use a higher
limit for hypertonic saline—a serum sodium level of 160
mmol/L and osmolality as high as 360 mOsm/L, although
some prefer the lower safety limits for both agents.
Of course, the appropriate thresholds would be those at which
sodium and osmolality are associated with greater
harm than the intracranial pressure they aim to treat.
In this context, there is a strong possibility that the ideal thresholds are specific to the patient and the situation.