

## Heterogeneity, evidence and salt

Lance Brown, MD, MPH

SEE ALSO PAGE 147.

In this edition of the *Canadian Journal of Emergency Medicine*, Vaillancourt and colleagues present an important article on acute compartment syndrome.<sup>1</sup> While reading this article I was struck by the heterogeneity of the subjects. I realized that I'd been naively thinking of "compartment syndrome" as a homogeneous entity. But these authors demonstrate that penetrating trauma, blunt trauma, and even non-traumatic problems funnel into a final common pathway that leads to acute compartment syndrome and fasciotomy. This prompted me to consider other heterogeneous conditions that are inappropriately viewed as homogeneous and to ponder the role that heterogeneity plays in the "evidence" used to make clinical decisions.

### Pediatric head trauma

Pediatric head trauma is heterogeneous in at least 2 fundamental ways. First, researchers frequently group "children" of all ages. In a recent observational study of traumatic brain injury,<sup>2</sup> Palchak and colleagues enrolled over 2000 "children," right up to 18 years of age. It seems intuitive to me that a 17-day-old, a 17-month-old, and a 17-year-old are different physiological creatures. A 17-day-old feeds and cries, a 17-month-old runs and plays, and a 17-year-old can drive a car, work for a living and conceive children. The authors performed recursive partitioning on their data and produced a list of low-risk criteria for traumatic brain injury. But, given the underlying heterogeneity of their subjects, I am uneasy using their decision rule to help me make decisions in the emergency department.

Second, the process of developing "evidence-based" guidelines often involves more than just "evidence." In

2001, Schutzman and colleagues suggested guidelines for the evaluation and management of children under 2 years of age with apparently minor head trauma.<sup>3</sup> In this proposed guideline the authors acknowledged that "available data do not demonstrate that either seizure, vomiting, or loss of consciousness are independent predictors for intracranial injury;" yet they proceeded to suggest that children with a seizure or loss of consciousness for longer than 1 minute should have computerized tomographic (CT) scanning of the head. With regard to vomiting, they arbitrarily suggested a threshold of 5 episodes or 6 hours of vomiting as an indication for a head CT. Why go to the trouble of reviewing many studies, which identify features not associated with intracranial injuries, and then recommend those exact features as indications for CT scanning? I believe the authors understand, on some level, that epidural hematomas, subdural hematomas, subarachnoid hemorrhages, depressed skull fractures, and other clinically important intracranial injuries are a heterogeneous group for which we should expect different clinical presentations. I remain open, however, to the possibility that this particular guideline might actually be eminence-based, vehemence-based, eloquence-based, providence-based, or nervousness-based.<sup>4</sup>

### Bronchiolitis

"Bronchiolitis" is not a disease; it is a convenient term for wheezing infants presumed to have viral lung infections. And it is heterogeneous. Studies<sup>5-7</sup> have demonstrated highly variable rates of respiratory syncytial virus infection in children with "bronchiolitis." Over the last decade there

From Loma Linda University Medical Center and Children's Hospital, Loma Linda, Calif.

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have been at least 9 randomized controlled trials evaluating the use of nebulized epinephrine to treat infants with bronchiolitis. Four of these suggested that epinephrine was efficacious,<sup>8-11</sup> 4 suggested it was not efficacious,<sup>12-15</sup> and 1 suggested that, although it might not be entirely efficacious, it might expedite discharge from the ED.<sup>16</sup> Not surprisingly, a subsequent meta-analysis concluded that epinephrine may have some minimal short-term benefits, but doesn't help inpatients.<sup>17</sup> The reality may be that bronchiolitis is a heterogeneous condition, that epinephrine works for some patients and doesn't work for others, and that when you study a heterogeneous clinical condition, the conclusions become muddled.

## Conclusion

In considering these examples, heterogeneity is probably pervasive and under-appreciated in clinical research. Unrecognized heterogeneity may have a profound impact on the conclusions of studies we use to guide clinical decision-making. "Evidence-based" medicine is wonderful fare, but when served with heterogeneity, readers should consider adding a "grain of salt."

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**Correspondence to:** Dr. Lance Brown, Department of Emergency Medicine, A-108, Loma Linda University Medical Center and Children's Hospital, 11234 Anderson St., Loma Linda CA 92354 USA; 909 558-4344, fax 909 558-0121, LBROWNMD@AOL.com