To the Editor

RE: Neuroscience in Nazi Europe Part III: Victims of the Third Reich. Can J Neurol Sci. 2012;39:729-746.

As the authors of this article,[1] we wanted to make a small annotation to "Table 1. Berlin Jewish Neurologists, deported and killed in Nazi concentration camps." The following line should be added regarding Dr. Ludwig Pick, who we also discuss in depth first in the Results section:

Pick, Ludwig	1868, Landsberg/ Warthe	N/A	Professor, Friedrichshain Hospital	16.6.1943	Theresienstadt, died 3.2.1944, pneumonia

In "Table 2: Viennese and Prague Neuroscience Victims of the Nazis," we erroneously did not list the source, which is the following:

Hubenstorf M. Tote und/oder lebendige Wissenschaft: Die intellektuellen Netwerke der NS-Patientenmordaktion in Österreich. In: Gabriel E, Neugebeauer W, editors. Von der Zwanssterilizierung zur ermordung: Zur geschichte der NS-euthanasie in Wien. Wien: Böhlau Verlag; 2002. p. 237-420.

Additionally, we did not notice that two Polish neurologist victims[2] were erroneously not included in "Table 3: Polish neurologist victims in the Third Reich." The following should be added to that table:

Arnold Birenbaum (1897-1942; neurologist in Warsaw, murdered by the Nazis)
Maksymilian Biro (1870-1941; died in the Warsaw Ghetto)

By including these additional Polish neurologists, we remember their names and honor them. Whether there are better ways to honor the neurologists who were victims of the Holocaust is a topic we hope will be debated following publication of our article.

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To the Editor

RE: Intracranial Pressure Monitors in Traumatic Brain Injury: A Systematic Review. Can J Neurol Sci. 2012;39: 571-576.

ICP Monitoring - Interpreting the Literature and Evaluating Practice

I read with interest the recent paper in your journal by Mendelson et al 'Intracranial pressure monitors in Traumatic brain Injury A Systematic Review'[1] and the accompanying editorial 'Technology in Caring for Traumatic Brain Injury: Does What Make Sense Really Do?'[2]. The authors are to be congratulated on contributing to the debate surrounding the use of intracranial pressure (ICP) monitors in traumatic brain injury (TBI). The major difficulty with this analysis of course, and which the authors recognize, is the quality of articles reviewed. The problem bedevilling the literature on ICP monitoring in trauma is the lack of randomized studies and the unequal groups that then get compared in observational, retrospective, or even worse – national database - studies, which account for all the articles reviewed here.

Unfortunately, the methodology of these studies is all too familiar – the comparison of those who were monitored for ICP versus those who were not; the clear problem being that patients who end up with an ICP monitor inevitably are very different from those who do not. Controlling for known factors that are associated with poor outcome is very important but does not necessarily make these two groups equivalent. The use of scoring systems is better than nothing but clinical decisions about whether a patient should receive a monitor are not based on these, and with all their individual limitations scoring systems also do not necessarily reveal the true injury severity, nor do they adequately predict the later risk of secondary injury[3].

The authors of the review acknowledge this 'confounding by indication'. Indeed, many factors influence the decision to place an ICP monitor, singly or in combination: clinical signs of increased ICP, secondary clinical deterioration, degree of brain swelling, intracranial hematoma, presence of major systemic injury, etc. It is highly unlikely that statistical tools adequately adjust for the true differences between patients or account for why an ICP monitor was placed. Inevitably the patients who received ICP monitoring are described as more severely injured, but the degree to which this is true is likely not completely apparent. The referenced article by Shafi et al[4] is an example of this: injury severity was greater in the ICP monitored group as was the number of patients who underwent craniotomy. Oddly, patients who died within 48 hours were excluded from analysis even though these patients may have benefited from ICP monitoring. A similar study in children suffers the same fate[5]: the ICP monitored group was more severely injured, had much higher requirements for ventilation, and needed central venous line insertion more often. The criticisms of these kinds of studies are extensive[6-8].

On the other hand, it is true that interventions based on ICP monitoring may harm a patient especially when used indiscriminately, and the ICP number alone provides little information about the underlying disturbance in the brain. The authors importantly draw a distinction between the information obtained from the ICP monitor and the interventions instituted

https://doi.org/10.1017/S031716710002254X Published online by Cambridge University Press

based on this information. I strongly agree with this – the use of aggressive and prolonged hyperventilation for increased ICP two decades ago is perhaps the best illustration of this principle: ICP was reduced, but at the expense of decreasing brain perfusion (presumably). Where I would slightly disagree though, is with their recommendation that for the device to improve outcome it has to be acted on in a standard and reproducible manner. In fact, this is a critical and contentious point at the heart of ICP monitoring. With the use of advanced monitoring and imaging, it is clear that increased ICP is not a single, homogeneous concept. Increased ICP may be associated with several different underlying physiological derangements, including cellular or vasogenic edema, impaired autoregulation (where increased blood pressure drives up the ICP), hyperaemia, subclinical seizures or spreading depression. Therefore, there is no physiological reason that ICP should respond in a standardized manner to specific interventions. The actual ICP is just a number. It does not reveal the underlying pathophysiology, so there is little rationale for why we have approached it in a standard manner or why it should respond as such. To be simplistic, a patient with increased ICP due to subclinical seizures needs seizure control not mannitol, and a patient with hyperaemia likely does not need a decompressive craniectomy. It would be not unlike using penicillin for a fever – in some cases it would be appropriate and helpful, in some no antibiotics are necessary, and in some an entirely different treatment may be needed.

The recent DECRA trial of decompressive craniectomy is an example of such standardized unfiltered treatment[9]. The treated group clearly had lower ICP and reduced ICU stay, but their outcomes were worse. In this study there was a questionable need for craniectomy in the treated group: the indication for surgery was incredibly low – the median ICP in the surgery group in the 12 hours before randomization was only 20 mmHg (interquartile range 18-22mmHg), which in most practices would not constitute an indication for craniectomy. As much as most clinicians agree that 20mmHg is a reasonable general treatment threshold, most would also agree that there has to be some balance between the degree of ICP elevation and the aggressiveness of therapy, the oft-discussed benefit/risk ratio. I do not suspect that for most working neurosurgeons who are familiar with craniectomy that this balances out at 20mmHg. As importantly, the group was likely heterogeneous for the above-mentioned reasons; additional monitoring may have revealed that for most of these patients perfusion to the brain was not impaired, neither was cellular metabolism. Arguably many patients ended up with a craniectomy who did not need one in the first place. Unfortunately, for many readers the take home message of this trial was that craniectomy does not work, a question that this trial cannot answer. This is perhaps a typical example of approaching a single ICP number, regardless of the underlying etiology and specific consequences of that ICP number, with a standard, unfiltered, and potentially harmful approach.

The same is true for cerebral perfusion pressure (CPP): we know that pressure autoregulation is often impaired in TBI patients; therefore, when autoregulation is impaired chasing an arbitrary target for CPP with circulatory support, ICP is pushed up further. However, this does negate the observation that in a patient with intact autoregulation, a higher CPP may actually be beneficial, but only if actually needed. If CPP was augmented in all patients in a standardized manner, the adverse effects would increase substantially[10]. More than likely, there is an optimal CPP in patients, rather than a one size fits all[11]. Even from our own experience with hyperventilation, although the response of ICP is predictable, the underlying changes to brain perfusion are not (unpublished data), presumably because the effect on perfusion of the decrease in ICP in some circumstances is greater than the flow limitation from the vasoconstriction. The key to all of the above is recognising the heterogeneity in patients with TBI.

From my perspective, ICP monitoring is valuable, but knowing how best to treat ICP (and how the brain responds to the treatment beyond the ICP number) depends on having more information at one's disposal. For me, this is the prime role of multimodality monitoring, i.e. not just having a new monitor to target a new threshold (such as brain oxygenation), but rather to improve our understanding of what we are already doing to individual patients, so that we can make more rational decisions. Some would say that we should not focus on multimodality monitoring if we cannot get ICP monitoring right. To this I would respond: it is only by getting more information about what is happening to the brain and about what we are doing to it, that we can ever get ICP monitoring right. If we were to achieve that, i.e. making more rational decisions and observing directly the effects of those decisions, then I believe that the technology we use in caring for patients with TBI will more likely make sense.

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