Primum non nocere

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[PII_REPLACE]

Primum non nocere: a call for balance when reporting on CTE

As clinicians and researchers in traumatic brain injury and neurodegeneration, we are concerned by the tone of reporting on chronic traumatic encephalopathy (CTE) that has developed over the past decade, highlighted in an article in *The New York Times*.[1] Misleading reporting can have unintended, negative consequences and we call for balance from the medical and scientific communities and the media when communicating on issues related to CTE.

Contrary to common perception, the clinical syndrome of CTE has not yet been fully defined,[2] its prevalence is unknown, and the neuropathological diagnostic criteria are no more than preliminary.[3] We have an incomplete understanding of the extent or distribution of pathology required to produce neurological dysfunction or to distinguish diseased from healthy tissue, with the neuropathological changes of CTE reported in apparently asymptomatic individuals.[4,5] Although commonly quoted, no consensus agreement has been reached on staging the severity of CTE pathology. A single focus of the pathology implicated in CTE is not yet sufficient evidence to define disease.

Recognising limitations of the diagnostic process in human pathology, pathologists are careful to note that they are merely providing an opinion, ~~and~~ acknowledging that another pathologist might reasonably reach a different conclusion on the same case.[6] In diagnoses where the criteria for assessment and reporting are established by broad consensus, the expectation is that variance in opinion is minimised. However, at this time, ~~although~~ CTE diagnostic criteria are far from established, discordance in opinions on individual cases is to be expected.[1]

Unfortunately, the uncertainties around the clinical syndrome and the pathological definition of CTE are not acknowledged adequately in much of the current research literature or related media reporting, which at times has resembled science by press conference.[7] Too often an inaccurate impression is portrayed that CTE is clinically defined, its prevalence is high, and pathology evaluation is a simple positive or negative decision. This distorted reporting on CTE might have dire consequences. Specifically, individuals with potentially treatable conditions, such as depression or post-traumatic stress disorder, might make decisions on their future on the basis of a misplaced belief that their symptoms inevitably herald an untreatable, degenerative brain disease culminating in dementia.

We propose that the principle of first, to do no harm, is used when communicating on CTE, whatever the platform. In particular, the many remaining uncertainties should always be acknowledged. Otherwise, the risk of doing harm is very real.

[A: Please declare any potential competing interests, and ensure these statements match your submitted ICMJE forms]

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1 Belson K. Doctors said hockey enforcer Todd Ewen did not have C.T.E. but he did. Nov 30, 2018. *The New York Times* https://www.nytimes.com/2018/11/30/sports/hockey/todd-ewen-cte-hockey.html?smtyp=cur&smid=tw-nytsports **[A: Please supply date accessed.]**

2 Wilson L, Stewart W, Dams-O'Connor K, et al. The chronic and evolving neurological consequences of traumatic brain injury. *Lancet Neurol* 2017; **16:** 813–25.

3 McKee A, Cairns NJ, Dickson DW, et al. The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy. *Acta Neuropathol* 2016; **131:** 75–86.

4 Ling H, Holton JL, Shaw K, et al. Histological evidence of chronic traumatic encephalopathy in a large series of neurodegenerative diseases. *Acta Neuropathol* 2015; **130:** 891–93.

5 Noy S, Krawitz S, Del Bigio MR. Chronic traumatic encephalopathy-like abnormalities in a routine neuropathology service. *J Neuropath Exp Neur* 2016; **75:** 1145–54.

6 Manion E, Cohen MB, Weydert J. Mandatory second opinion in surgical pathology referral material: clinical consequences of major disagreements. *Am J Surg Pathol* 2008; **32:** 732–37.

7 Moore A. Bad science in the headlines. Who takes responsibility when science is distorted in the mass media? *EMBO Rep* 2016; **7:** 1193–96.