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Title: Updates in Chronic Traumatic Encephalopathy (CTE): - What Are the Critical Questions?

Abstract: Chronic traumatic encephalopathy (CTE) is a neurodegenerative tauopathy associated with repetitive mild head trauma, including concussion and asymptomatic subconcussive impacts. CTE was first recognized in boxers almost a century ago and has been recently identified in contact sports athletes, including players of American football, ice hockey, soccer, baseball, rugby, boxing, and wrestling, military veterans exposed to blast, and victims of domestic violence. Like most neurodegenerative diseases, CTE is diagnosed conclusively only by neuropathological examination of brain tissue. CTE is characterized by the buildup of hyperphosphorylated tau (p-tau) as neurofibrillary tangles (NFTs), abnormal neurites and inclusions in astrocytes that occur around small blood vessels with a tendency to occur in clusters at the sulcal depths of the cortex. The largest clinicopathological series of CTE to date was reported in 177 former American football players, including 110 of 111 former NFL players (99%), 48 of 53 former college football players (91%) and 3 of 14 former high school players (21%). There is a significant relationship between the length of playing career and pathological severity of CTE, as well as between ptau pathology, inflammation, and dementia, and age at death. Recently, BU CTE Center researchers reported that the risk and severity of developing CTE increases with the number of years playing American football. In a sample of 266 deceased former amateur and professional football players, the study found that the risk of developing CTE increased by 30 percent per year played, meaning that for each 2.6 additional years of football played, the odds of developing CTE doubled. Among those with CTE, for each additional 5.3 years played, the odds of developing severe CTE doubled. Dr. McKee will discuss how CTE begins in the brain, how it spreads over time and what symptoms it causes. She will tell the histories of several individuals diagnosed with CTE whose brains were donated to the CTE Center. Although tremendous advances have been made over the past decade, there remains an urgent need to develop biomarkers to identify CTE during life and to develop effective therapies for people suffering from the disorder.

Bio: Ann McKee, MD, is a William Fairfield Warren Distinguished Professor of Neurology and Pathology at Boston University School of Medicine, Director of Neuropathology for VA Boston, and Director of the BU Chronic Traumatic Encephalopathy (CTE) Center. Dr. McKee is a board certified neurologist and neuropathologist whose initial career focused on Alzheimer's disease and aging. Over the past 10 years, she has concentrated on the long-term effects of concussion, subconcussion and blast injury and CTE in contact sports athletes and military veterans. Her work has shifted the prevailing paradigm of scientific thought regarding head trauma; she demonstrated that repetitive "mild" head trauma is not just an acute injury, it can provoke a persistent neurodegeneration, CTE, that continues long after the trauma has stopped. Dr. McKee has published over 80% of the world's cases of CTE ever reported and created the UNITE (VA-BU-CLF) brain bank, the world's largest repository of brains from individuals exposed to traumatic brain injuries (over 780) and neuropathologically confirmed CTE (over 400). McKee completed her undergraduate studies at the University of Wisconsin and received her medical

degree from the Case Western Reserve School of Medicine. She completed her residency training in neurology at Cleveland Metropolitan General Hospital and in neuropathology at Massachusetts General Hospital. She is Director of the Neuropathology Core and Associate Director for the Boston University Alzheimer's Disease Center (BUADC). McKee also directs the brain banks for the BUADC and Framingham Heart Study which are based at VA Boston. McKee was named Bostonian of the Year 2017 by the Boston Globe, one of the 50 Most Influential People in Healthcare and one of the 100 Most Influential People in the World by Time magazine in 2018. She was recently awarded the Henry Wisniewski Lifetime Achievement Award in Alzheimer's Disease Research by the Alzheimer's Association, was elected into the National Academy of Medicine and received the Samuel J. Heyman Service to America Medal (Sammie), Paul A. Volcker Career Achievement Award for outstanding contributions to federal service.