NEUROLOGICAL CONSEQUENCES
OF COMBAT SPORTS

PROGRAM SYLLABUS
Chronic traumatic brain injury represents a spectrum of disorders associated with long term consequences traumatic brain injury (Table 1). The prototype of CTBI is chronic traumatic encephalopathy (CTE) (1). CTE represents the long term neurological consequences of repetitive mild traumatic brain injury. Dementia pugilistica represents the boxing manifestation of CTE but is typically reserved for the cases of severe dementia following a long boxing career.

**Chronic Traumatic Encephalopathy**

Chronic traumatic encephalopathy (CTE) long term neurologic consequences of repetitive concussive and subconcussive blows to the head presumed to be secondary to a progressive tauopathy (2,3). This syndrome was first described in the medical literature by Martland in 1928 when he described a 38-year old retired boxer with advanced parkinsonism, ataxia, pyramidal tract dysfunction, and behavioral changes (4). CTE is typically delayed in onset and occurs after a long exposure to the sport, usually after a boxer retires or late in the career of a boxer. As a result of this delayed onset, CTE represents the most difficult safety challenge in modern day boxing.

The true incidence and prevalence of CTE in the modern era boxing is unknown. Among ex-professional boxers who were licensed by the British Board of Control for at least 3 years from 1929 through 1955, it has been estimated that the prevalence of CTE is 17 % and the prevalence increases with increasing exposure to boxing (5). However it has been speculated that the risk of CTE will diminish secondary to the reduction in exposure to repetitive head trauma and increasing medical monitoring of boxers (6). Strong objective evidence linking CTE with amateur boxing has lacking (7). More recently it has been suggested that modern era CTE differs from what has been described in the past (8).

Putative and established risk factors for CTE are presented in Table 2. Increased exposure probably represents the most important risk factor for CTE. Documented risk factors for CTE in boxing include later retirement (i.e., over 28 years of age), increased duration of career (i.e., more than 10 years), and a greater number of bouts (i.e., more than 150 bouts) (5). Other putative risk factors for the development of CTE among professional boxers include poor performance (i.e. second- or third-rate boxers), boxing style (i.e., being a slugger, rather than a scientific, intelligent boxer), boxers who are notorious for their ability to “take” a punch, and being a professional boxer as opposed to amateur (5). The age at examination also influenced the prevalence of CTE. Boxers who were examined after the age of 50 had a higher prevalence of CTE than those examined before that age of 50 (5). Increasing sparring exposure may increase the risk of neuro-cognitive decline among professional boxers (9). A history of a TKO or KO has also been reported to be associated with an abnormal computed tomographic (CT) scan of the brain.
In addition, progressive changes on CT scans have been noted in boxers who lose more than 10 bouts (11).

MRI surveillance of active professional boxers have found associations between boxing history and abnormalities on MRI. Boxers exhibiting a cavum septum pellucidum (CSP) (a common radiological finding among boxers with long exposure to boxing) on MRI tended to experience more losses, more TKO/KO’s, and medical suspensions (12). Boxers with white matter changes on MRI (which are non-specific and potentially related to brain trauma) were also noted to have an increased frequency of losses (12). Orrison et al. utilizing high field MRI to evaluate 100 unarmed combatants (boxers and mixed martial artists) observed a statistical association between the number of bouts and increased lateral ventricular size (13). These investigators also observed that combatants with longer careers more frequently exhibited dilated perivascular spaces (possible evidence suggestive of DAI).

In a comprehensive review of the neuropsychiatric aspects of boxing, Mendez (14) classified the clinical manifestations of CTBI into motor, cognitive, and psychiatric symptoms. Early signs of CTE may include dysarthria, mild incoordination, tremor, and decreased complex attention. Psychiatric symptoms may include emotional lability and other mild behavioral disturbances such as euphoria or hypomania and increased irritability. Although it has been observed that the initial manifestations of CTE are predominantly psychiatric or behavioral in nature (15), it is the experience of the author that the behavioral and personality disturbances may be difficult to assess early in the disease. This is particularly the case when the examiner lacks knowledge of the boxer’s premorbid personality. The second or moderate stage of CTE is characterized by a progression of the motor, cognitive, and/or behavioral symptoms (14). Motorically, boxers exhibit signs of parkinsonism and/or progressive difficulty in coordination and ambulation. Cognitive deficits include mild deficits in memory, attention, and executive function. Psychiatric manifestations may include inappropriate behavior, morbid jealousy, paranoia, and violent outbursts. The third or severe stage of CTBI is often referred to as dementia pugilistica (14). During this phase of the disorder, the boxer exhibits significant motor dysfunction characterized by prominent pyramidal, extrapyramidal, and/or cerebellar symptoms. Cognitive dysfunction as evidenced by amnesia, executive-frontal lobe dysfunction, and psychomotor retardation may be observed. Behaviorally, boxers may exhibit disinhibition, violent outbursts, hypersexuality, and psychosis (14).

In addition to a detailed neurological examination documenting cognitive, behavioral and/or motor impairments in a boxer, various neurodiagnostic tests have been utilized in the evaluation of the boxer with suspected CTE. Structural neuroimaging demonstrates nonspecific findings in CTE. Computed tomography (CT) and magnetic resonance imaging (MRI) may demonstrate brain atrophy with or without a cavum septum pellucidum (10-13, 16-21). Diffusion tensor imaging (DTI) can document injury to the white matter tracts among active boxers (21). More recently, Banks et al. (22) documented that increased exposures to boxing and MMA were associated with reduced caudate and amygdalar volumes.

The utilization of functional neuroimaging in boxing and the MMA has been relatively limited. Single photon emission computed tomography (SPECT) may exhibit perfusion deficits in boxer (23, 24) that localize primarily to the frontal and temporal regions (24). Positron emission tomography (PET) scanning may demonstrate hypometabolism in the bilateral posterior parietal lobes, bilateral frontal lobes, bilateral cerebellar hemispheres, and posterior cingulate gyrus (25). Amyloid PET scans may be useful in ruling out an Alzheimer’s type process which can potentially narrow the differential diagnosis of CTE. Magnetic resonance spectroscopy (MRS) provides a non-invasive means of identifying neurometabolic changes of the brain indicative of neuroinflammation (26).

Pathologically, CTE has been described as a distinct pathological entity that is distinguishable from other dementias (2,3) Boxers with endstage CTE or full blown dementia pugilistica may exhibit septal and hypothalamic anomalies, cerebellar changes, degeneration of the substantia nigra, and regional occurrence of Alzheimer’s neurofibrillary tangles (NFT) (2,3,27,28). Boxers may exhibit a fenestrated
septal cavum, the floor of the hypothalamus may appear to be stretched, and the fornix and mammillary bodies may be atrophied. The cerebellum may demonstrate scarring of the folia in the region of the cerebellar tonsils, and there may be a reduction in the number of Purkinje cells on the inferior surface of the cerebellum. The substantia nigra may lack pigment, and nerve cells may become gliosed. The histological hallmark of CTE is hyperphosphorylated tau pathology ranging in severity from focal perivascular epicenters of NFT in the frontal cortex to severe tauopathy widely distributed throughout the cerebral cortex, diencephalon, basal ganglia, brainstem and spinal cord (3). NFT are not typically accompanied by senile neuritic plaques but may be accompanied by diffuse amyloid plaques (2,3,29,30). NFT observed in boxers with CTE are also immunoreactive for tau (30) and ubiquitin (31). CTE, similar to Alzheimer’s disease (AD) may exhibit a significant reduction of choline acetyltransferase activity in the nucleus basalis of Meynert (nbM) and in several regions of the cerebral cortex (32). Uryu et al. (33) in an animal model of TBI noted that TBI induces the rapid accumulation of key proteins that form pathologic aggregates in neurodegenerative disorders. Kokjohn and colleagues (34) have noted disturbances in the expression and processing of glial fibrillary acidic protein (GFAP), tau and α synuclein as well as a reduction in neprilysin, an amyloid degrading enzyme.

**Conclusion**

CTE represents an important public health concern in modern day contact, collision and combative sports. Until, in vivo diagnostic tests become available, prevention of CTE is of paramount importance. The mainstay of preventing CTE in boxing and the combat sports is to limit exposure and identify those boxers and mixed martial artists that may be at increased risk of CTE. Boxers that may be at increased risk of CTE (table 2) should undergo more detailed neurodiagnostic testing such as MRI, SPECT, PET and neuropsychological testing. Although APOE genotype may be associated with more neurological impairment in active and retired boxers (35), whether APOE genotyping will prove useful in the prevention of CTE remains to be determined, but represents an extremely controversial topic (36). Theoretically, boxers that are APOE e4 positive can be informed their potential risks and followed more closely for the neurological standpoint. Until advances in tau imaging is achieved, the diagnosis can only be accomplished at postmortem.

**REFERENCES**

Table 1: Classification Chronic Traumatic Brain Injury

- Chronic Traumatic Encephalopathy
- Dementia Pugilistica
- Chronic Postconcussion Syndrome
- Chronic Neurocognitive Impairment
- Posttraumatic Parkinsonism (including pugilistica parkinsonism)
- Posttraumatic Dementia
- Posttraumatic Cognitive Impairment

Table 2: Putative and Documented Risk Factors for Chronic Traumatic Encephalopathy in Boxing

- Total number of fights
- Number of knockouts experienced
- Number of losses
- Duration of boxing career
- Fight frequency
- Age of retirement from boxing
- Sparring exposure
- Poor performance or skills
- APOE ε4 genotype

Table 3: Clinical Presentation of Chronic Traumatic Encephalopathy

Behavioral/Psychiatric
- Aggression/Agitation
- Apathy
- Impulsivity
- Depression
- Delusions (e.g. paranoia)
- Suicidality

Cognitive
- Impaired attention/concentration
- Memory problems
- Executive dysfunction
- Dementia
- Visuospatial difficulties
- Language impairment

Motor
- Dysarthria, scanning speech
- Spasticity
- Ataxia, incoordination
- Parkinsonism, tremors
- Gait disturbance
- ? Motor neuron disease