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Repetitive Repetitive Repetitive Repetitive brain injury & CTE

Last year, it was announced that chronic traumatic encephalopathy (CTE) was identified in 87 out of 91 former NFL players, or 96%, garnering media attention and shining a light on this disease.

By Amanda Perkins, MSN, RN

CTE is an irreversible neurodegenerative disease seen in individuals who've experienced recurring traumatic brain injury (TBI). CTE is most commonly observed in athletes with a history of repetitive TBI. The following activities have been associated with CTE:

- military service
- football
- hockey
- wrestling
- rugby
- soccer
- lacrosse
- downhill skiing
- martial arts
- horseback riding
- parachuting.

Physical abuse and epilepsy also put individuals at risk.

It's believed that recurring TBI can cause accumulation of the protein tau and progressive degeneration of brain tissue (see *Disintegration of microtubules in neurons*). Although it's well established that CTE and TBI are related, questions exist about possible correlations with environmental factors, such as performance-enhancing drugs, alcohol, opioids, and psychological stress.

In this article, we discuss the brain anatomy and physiology affected by CTE; its signs and symptoms, diagnosis, and associated conditions; and your role in prevention.

A&P asap

The following are abnormal findings observed on gross examination in patients with CTE:

- anterior cavum septum pellucidum
- enlargement of the lateral and third ventricles
- thinning of the corpus callosum
- scarring of the cerebellum
- shrinkage of the thalamus, hypothalamus, and mammillary bodies

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• pallor of the substantia nigra
• hippocampal sclerosis
• atrophy of the cerebrum, diencephalon, basal ganglia, brainstem, and cerebellum.

The cavum septum pellucidum is a crevice-like space that's found between the left and right transparent septum. This area in the brain has been called the fifth ventricle, although it has no direct communication with the ventricular system. The cavum septum pellucidum is a normal finding in a fetus, appearing in the fourth month of development, but should degenerate in infancy. The presence of a cavum septum pellucidum in adults has been associated with CTE. It's believed that repetitive brain trauma causes fluid waves within the ventricles that damage the septum pellucidum, causing the leaflets of the septum pellucidum to separate and creating a space that fills with cerebral spinal fluid (CSF).

did you know?

CTE has been described in the medical literature since as early as 1927. Throughout the years, CTE has been known by a variety of names, including traumatic encephalitis, punch drunk, dementia pugilistica, and traumatic progressive encephalopathy. The following is a brief outline of the history of CTE:

- 1927—Physicians Michael Osnato and Vincent Gilberti first introduced the idea that chronic neurodegeneration could occur as the result of brain trauma. They termed the changes that they observed *traumatic encephalitis*.
- 1928—A psychologist and medical examiner named Harrison Martland described changes that occurred in professional pugilists (boxers) after repeated blows to the head. He termed the changes that he observed *punch drunk*.
- 1937—The physician J.A. Millspaugh described a disease that occurred in boxers after sustaining repeated blows to the head. He termed this disease *dementia pugilistica*.
- 1950s–1970s—The term *chronic traumatic encephalopathy* was first used by the neurology professor Henry Miller in the literature in 1966.
- 1973—Detailed descriptions of the clinical and neuropathic features of CTE were developed by John Arthur Nicholas Corsellis, a professor who studied the brain, specifically neuropsychiatric disease. These descriptions helped form the pattern of structural brain abnormalities that are seen in CTE.
- 2002—CTE was discovered during forensic neuropathologist Bennet Omalu's autopsy of former NFL player Mike Webster.
- 2005—Dr. Omalu published his findings, describing the pathology of CTE.

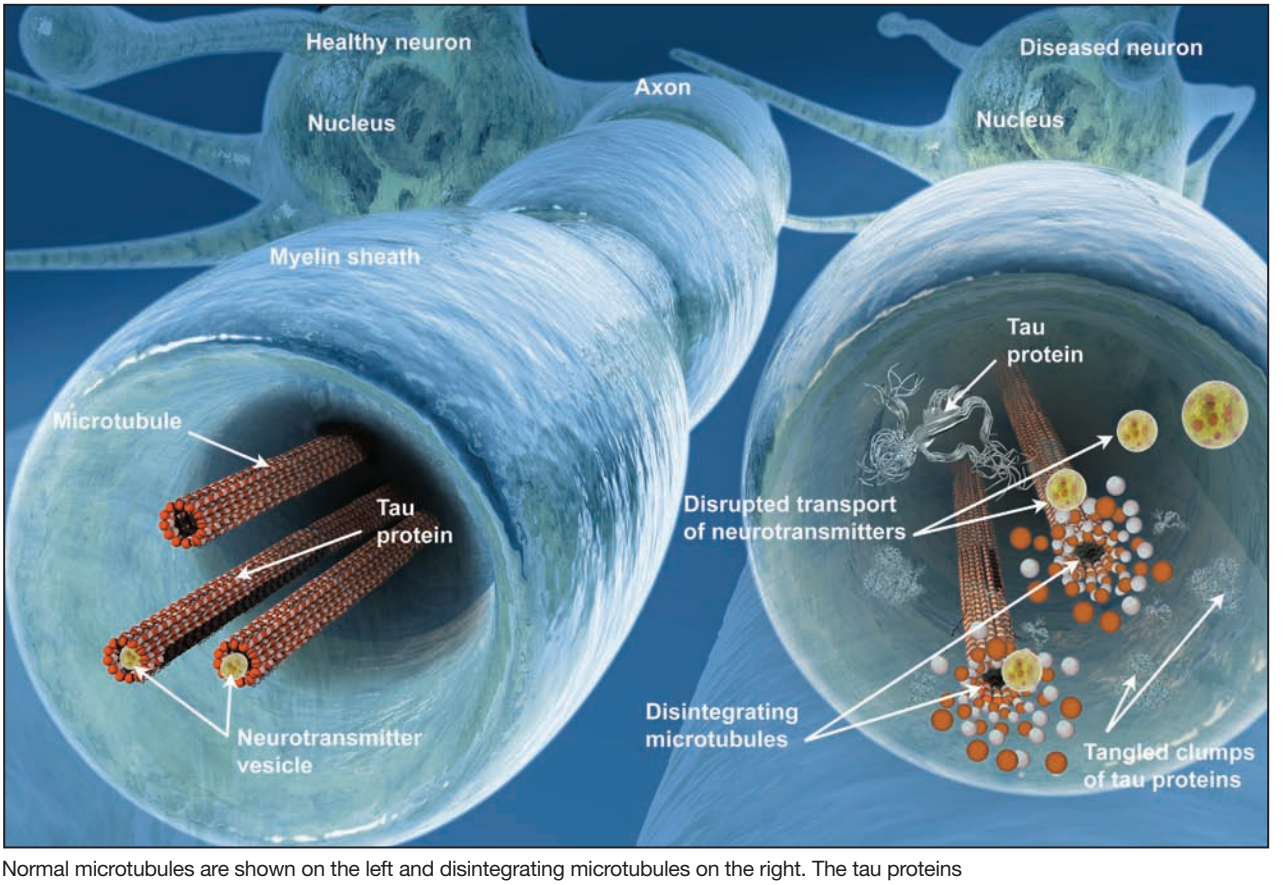
The ventricles are fluid-filled spaces found deep within the brain. Richly supplied with blood vessels, they play a critical role in the production and circulation of CSF. There are four ventricles in the brain: the paired lateral ventricles found in the cerebral hemispheres, the third ventricle found in the midline of the diencephalon, and the fourth ventricle found in the brainstem. In CTE, enlargement of the lateral and third ventricles occurs. Brain injury edema can occur, which may cause increased intracranial pressure and, in turn, ventricle expansion. Ventricle enlargement can also occur as a result of brain atrophy, which creates more room for the ventricles to expand.

The corpus callosum is an important structure because it connects the two sides of the brain. It's a 250- to 300-million axon bundle that allows both sides of the brain to communicate. A cut to the corpus callosum would result in two independent hemispheres, meaning that each side of the brain would only be aware of half of the body. With CTE, the corpus callosum becomes thinner, possibly as the result of neuronal loss.

The cerebellum, also known as the little brain because its appearance resembles the brain, is found on the back of the brainstem. Responsible for muscle activity, balance, and equilibrium, it's also hypothesized that the cerebellum plays a role in thought, emotion, and language. In patients with CTE, cerebellar scarring may be present. This scarring occurs as the result of neuronal loss. As neurons die in the brain, scar tissue is formed.

The thalamus consists of a pair of egg-shaped structures responsible for relaying, receiving, and processing information, and then sending the collected information to the cerebral cortex. The hypothalamus, found below the thalamus, plays an important role in controlling automatic functions, such as BP, heart rate, respiratory rate, and temperature; endocrine system glands; and behaviors associated with survival, such as eating and drinking. The hypothalamus is also vital for the maintenance of homeostasis. The

Disintegration of microtubules in neurons



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Normal microtubules are shown on the left and disintegrating microtubules on the right. The tau proteins binding the microtubules break down and form tangled masses, which are thought to contribute to Alzheimer disease and possibly CTE. Additionally, the flow of neurotransmitters to the synaptic membrane is disrupted.

mammillary bodies are a part of the limbic system, a group of interconnected structures that are central to emotions and memory. In patients with CTE, there may be shrinkage of the thalamus, hypothalamus, and mammillary bodies as a result of neuronal loss.

The substantia nigra is found in the basal ganglia and is a key component of the motor system. The neurons responsible for the production of dopamine—a significant neurotransmitter for movement and emotional response—are found in the substantia nigra. Pallor of the substantia nigra is seen in individuals with CTE due to degeneration.

The hippocampus is found in the temporal lobe and is essential for memory. It plays a chief role in the development of new memories and, to some degree, the maintenance of old memories. In patients with CTE, hippocampal sclerosis occurs. With repetitive brain injuries, there's a loss of neurons. The death of these neurons leads to the formation of scar tissue in the hippocampus.

Patients with CTE will develop atrophy in a variety of areas in the brain. Atrophy of the cerebrum, diencephalon, basal ganglia, brainstem, and cerebellum results in a reduced brain weight. Basically, atrophy is a loss of cells; more specifically, a loss of neurons and their connections. This loss of cells can lead to impaired memory, cognitive dysfunction, and impaired voluntary processes.

At a microscopic level, CTE can be characterized by neurofibrillary tangles, neutrophil threads, and glial tangles. The neurofibrillary tangles seen in individuals with CTE are believed to be associated with tau, a protein in the brain that helps stabilize and support brain cell structures. After repeated brain injuries, the tau protein becomes misshapen. Once the shape of the tau protein changes, it's released into brain cells and causes a chain reaction that leads to clumping of the protein. These clumps eventually kill neurons. When compared with other tau pathologies, such as Alzheimer disease, the tau protein pattern seen with CTE is unique because it's irregular and found in different areas of the brain.

Beta-amyloid is a protein fragment found in the fatty membrane surrounding nerve cells. These fragments are sticky and, as a result, clump together, blocking cell signaling at the synapses. Beta-amyloid deposits—the same seen in Alzheimer disease—are found in nearly half of individuals with CTE. Although this is a high number, it differs from Alzheimer disease because beta-amyloid is found in nearly all individuals with Alzheimer disease.

In addition to tau and beta-amyloid, the phosphorylated protein TDP-43 has been observed in cases of CTE. It's believed that repetitive axonal injury causes the accumulation of TDP-43, which has been associated with the neurodegeneration seen in CTE.

consider this

A 43-year-old male patient arrives at the physician's office with his wife of 20 years. The patient and his wife report that they're concerned because, within the last year, he's had worsening personality changes. The patient indicates that he becomes angry easily and is finding it increasingly difficult to control his emotions. He states that when he gets angry, he throws items in the house and has broken walls and doors. Both he and his wife remark that they're concerned his outbursts may escalate to physical violence. Additionally, his wife notes that he's been making poor financial decisions, such as purchasing new vehicles without discussing it with her. Due to his impulse buying, they're financially strained. They tell you that in the past, he was always very conscientious about money and focused on saving rather than spending. During your patient history, you learn that the patient played football from grade school through college and sustained multiple concussions during that time.

Signs and symptoms delay

The signs and symptoms associated with CTE may not be observed until months, years, or even decades after a brain injury. In many cases, patients may not display any signs or symptoms of CTE until they're in their 40s. When symptoms do develop early on, they typically include behavioral changes. The signs and symptoms associated with CTE include:

- impaired judgment
- impulse control problems
- aggression
- impaired reasoning
- impaired problem solving
- memory loss
- confusion
- depression
- dementia
- anxiety
- impaired cognition
- suicidal tendencies.

With CTE, some of the most damaged areas of the brain are the medial structures of the limbic system, such as the amygdala, hippocampal-entorhinal complex, basal forebrain, and mammillary bodies. Scattered changes are also seen throughout the cerebral cortex. The changes that occur in the limbic system and cerebral cortex are responsible for the cognitive impairment and dementia that's seen in individuals with CTE.

CTE has been associated with a decline in short-term memory, similar to the memory loss that's observed in patients with Alzheimer disease. The memory loss seen in CTE may be a result of the buildup of tau protein in the medial temporal lobe structures that are responsible for the encoding and storage of new information.

In patients with CTE, executive function may be impaired, causing poor insight, judgment, and disinhibition. Executive functioning is controlled by the frontal lobes and the connections they make with other areas of the brain. In individuals with CTE, frontal lobe atrophy, neuronal loss, and neurofibrillary tangles cause executive function loss.

Mood, personality, and behavioral changes are common. Changes seen in these patients may include aggression, violence, confusion, dysphoria, paranoia, irritability, agitation, apathy, hypersexuality, depression, and suicidality.

Individuals with CTE may have an altered sense of smell due to neurofibrillary changes in the olfactory bulb. These changes are similar to those seen in Alzheimer disease and Parkinson disease.

The diagnostic situation

A definitive diagnosis of CTE can't be made until a patient dies and an autopsy can be performed. However, the following tests may be utilized when diagnosing a patient with suspected CTE:

- magnetic resonance imaging (MRI)
- susceptibility-weighted imaging (SWI)
- diffusion tensor imaging (DTI)
- magnetic resonance spectroscopy (MRS)
- event-related potentials (ERPs)
- positron emission tomography (PET)
- single-photon emission computed tomography (SPECT)
- blood and CSF biomarkers.

An MRI may detect changes commonly observed in patients with CTE, such as brain atrophy and cavum septum pellucidum.

SWI can detect microhemorrhages in the brain after physical trauma. SWI is a diagnostic tool that shows promise, but more research needs to be conducted to determine its usefulness in diagnosing CTE. It's hoped that SWI may be helpful in detecting perivascular tau deposits seen in patients with CTE.

DTI, a type of MRI, can detect axonal injury, which is commonly seen in patients with TBI. DTI is another imaging technique that requires more research to determine its effectiveness in diagnosing CTE, but it does show promise.

MRS is a noninvasive way to measure human brain chemistry, such as the alterations in brain metabolism that can occur with brain injuries.

There's ongoing research regarding ERPs and their effectiveness in detecting CTE. In the future, ERPs may be used to detect the neurophysiologic changes that are associated with memory difficulties occurring as the result of brain injuries.

PET scans are used to map the location of specific molecules within the brain. This may be useful in diagnosing CTE because PET ligands can nonselectively bind to tau, which is seen in the brains of individuals with CTE. At this time, specific PET markers for tau are being developed. PET ligands that selectively bind to tau may be particularly valuable in detecting CTE.

There are ongoing studies regarding SPECT and its utility in detecting CTE. SPECT is able to measure regional cerebral blood flow, but may not have the specificity required to note the tau-based changes seen with CTE.

Blood and CSF biomarkers may be beneficial in detecting the

key points

- CTE is an irreversible, progressive disease that's a complication of recurring TBI.
- The signs and symptoms of CTE may not be observed until years after a brain injury.
- When symptoms develop early, they typically include behavioral changes.
- A definitive diagnosis can only be made after death via autopsy.
- CTE can't be reversed or cured, so interventions are aimed at prevention and recognition of head injuries.
- Nursing care for the patient with CTE is similar to the care of patients with dementia.

neurodegenerative changes associated with CTE. It's believed that some of the biomarkers used in Alzheimer disease research may prove useful for CTE diagnosis. Research into blood and CSF biomarkers is still in its infancy and more work needs to be completed before we know how these will work in detecting CTE.

CTE in the news

- February 2011—Former NFL player Dave Duerson commits suicide with a gunshot wound to the chest instead of his head so that his brain can be examined for CTE. After an autopsy, it was determined that he did have CTE.
- April 2012—Former NFL player Ray Easterling commits suicide. During an autopsy, signs of CTE were discovered.
- June 2012—A lawsuit was filed accusing the NFL of negligence and failing to educate players about the link between concussion and brain injuries.
- September 2012—The NFL commits to donating $30 million to promote research on medical conditions commonly found in athletes.
- August 2013—The NFL and ex-players reach a deal in the class action lawsuit. As a result, the NFL has to pay $765 million.
- October 2013—*Frontline* airs *League of Denial: The NFL's Concussion Crisis*, a 2-hour special about the hidden story of the NFL and brain injury.
- October 2013—*League of Denial: The NFL, Concussions, and the Battle for Truth*, written by Mark Fainaru-Wada and Steve Fainaru, is published.
- September 2015—The Department of Veteran's Affairs and Boston University announce that 87 out of 91 former NFL players examined are found positive for CTE.
- January 2016—CBS publishes a news story that Dr. Omalu believes OJ Simpson has CTE.
- March 2016—The NFL acknowledges a link between football and CTE.

By association

Conditions that have been associated with CTE include:

- Alzheimer disease
- Lewy body disease
- frontotemporal lobe degeneration
- motor neuron disease.

It's believed that the presence of one or more of these diseases may increase the chances of developing another.

The most common type of dementia, Alzheimer disease is a progressive degenerative brain disease. The patient with Alzheimer disease experiences memory impairment, difficulty reasoning, and an inability to perform daily tasks.

Lewy body disease is a progressive dementia that occurs as the result of abnormal microscopic deposits that damage brain cells. It's the third most common type of dementia. The patient with Lewy body disease experiences difficulty with thinking and reasoning, confusion, memory loss, hallucinations, delusions, and Parkinson disease symptoms.

Frontotemporal lobe degeneration is the second most common cause of early-onset dementia. The patient with frontotemporal lobe degeneration will display socially inappropriate behaviors, such as disrobing and making sexual advances, followed by movement difficulties in the later stages.

Motor neuron disease affects the motor nerve cells of the spinal cord, brainstem, and cerebral cortex. Patients with motor neuron disease will lose motor control, eventually becoming paralyzed while their personality and mind remain intact.

Research suggests that trauma may be a risk factor for the development of these conditions. More research is needed to determine their correlation with CTE.

Prevent to protect

Medical interventions aren't available to halt the progression of CTE. Because CTE can't be reversed once present, your nursing interventions should be aimed at

preventing the initial trauma that leads to CTE development.

Although more research is needed, it's believed that the prevention of CTE should be centered on the avoidance of repetitive TBIs. It's important to be aware that certain circumstances, such as those involving military personnel and high-risk sports like boxing and football, may place individuals in situations in which repetitive brain injuries can't be completely prevented (see *CTE in the news*). When individuals are in situations in which blows to the head are unavoidable, prevention should focus on concussion assessment and management, which may prevent long-term consequences such as CTE.

Other preventive methods may include limiting the number of full-contact practices for sports with a high risk of head injury; implementing rules of play that decrease the risk of head injury, such as the rule that bans helmet-to-helmet collisions in the NFL; and increasing the use of appropriate protective headgear in contact sports.

It's also imperative to prevent TBI in children and adolescents because they're more vulnerable to head injury and potentially CTE as a result. The brain isn't fully developed until an individual is in his or her 20s; theoretically, brain injuries before that time may cause more damage and an increased risk of long-term complications.

Nursing care

Caring for a patient with suspected CTE entails supportive care, similar to patients with dementia. Provide a calm environment free from unnecessary clutter and distracting noises. This may help reduce confusion and negative behaviors.

Communicating effectively with patients with suspected CTE is essential. Ineffective communication can lead to agitation and negative behaviors. Maintaining a structured routine is important because it will help decrease confusion and frustration.

on the web

Alzheimer's Association:
www.alz.org/dementia/chronic-traumatic-encephalopathy-cte-symptoms.asp

CDC:
http://www.cdc.gov/concussion/HeadsUp/clinicians/resource_center/complications_of_concussion.html#five

Concussion Legacy Foundation:
http://concussionfoundation.org/learning-center/what-is-cte

Frontline:
http://www.pbs.org/wgbh/frontline/article/the-four-stages-of-cte/

Mayo Clinic:
www.mayoclinic.org/diseases-conditions/chronic-traumatic-encephalopathy/basics/definition/con-20113581

Encourage your patients to be as independent as possible for as long as possible. One of the best ways to help your patient maintain independence is by breaking tasks into small, manageable steps. Encouraging your patient to exercise should be a priority because exercise has been shown to improve mood and sleep, decrease signs and symptoms of depression, retain motor skills, and prevent constipation. Engaging patients in games or other activities that promote cognitive function may help delay mental decline.

An unfolding investigation

Research regarding CTE is ongoing and there are many questions left unanswered. Continue to review evidence-based findings as they're available to help your patients stay safe. ■

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