

# ANSWERING QUESTIONS ABOUT Chronic Traumatic Encephalopathy (CTE)

## INFORMATION FOR HEALTHCARE PROVIDERS



This fact sheet discusses information based on the latest science about CTE, including clinical presentation, risk factors, diagnosis, and strategies for speaking with patients. Research on CTE is emerging, and more studies are needed to fully answer questions about the disease.

## Understanding CTE

CTE is a neurodegenerative disease that is associated with changes and deficits in cognition, behavior, mood, and motor skills. It is believed to be caused in part by exposure to *repetitive* head impacts, including concussions as well as subconcussive trauma (i.e., head impacts that do not cause symptoms of concussion).<sup>1</sup>

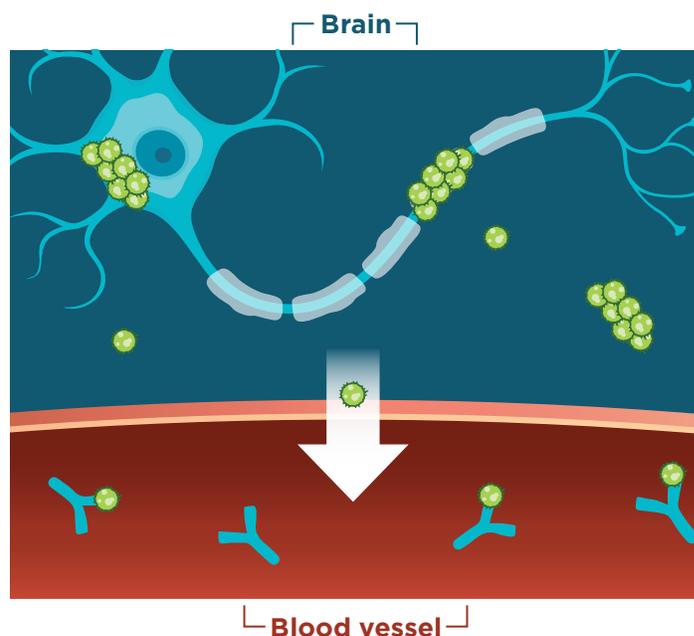
It is believed that repetitive head impacts set in motion a complex set of events in the brain. Primary among these are changes in the white matter (the brain's connecting wires) and the accumulation of an abnormal, hyperphosphorylated form of tau protein (p-tau). Scientists believe that the p-tau eventually spreads throughout much of the brain, leading to widespread neurodegeneration.<sup>2</sup>

## Timeline of Events in the Study of CTE

CTE was first described almost 90 years ago when its symptoms were observed in boxers. Although knowledge of the neuropathology of CTE has grown significantly, and media attention toward the disease has increased, the scientific understanding of CTE is still in its early stages.<sup>3</sup>

The timeline on the next page describes important moments in the study of CTE.

### Mechanism of Tau Protein Capture



The protein tau (green) aggregates abnormally in a brain cell (blue). Tau spills out of an injured cell and enters the bloodstream (red). Research shows that antibodies (blue) can capture tau in the blood that reflect its levels in the brain.

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SOURCE: National Institutes of Health Director's Blog, "Antibody Makes Alzheimer's Protein Detectable in Blood," May 2017

## Timeline of Key Events in the Study of CTE

<b>1928–1937</b>	CTE is first described in boxers as “punch drunk” <sup>4</sup> and later as “dementia pugilistica.” <sup>5</sup>
<b>1949–1957</b>	The term “chronic traumatic encephalopathy” is first used in the scientific literature. <sup>6,7</sup>
<b>1973</b>	The neuropathology of CTE is first described in a series of boxers. <sup>8</sup>
<b>2005</b>	A case study is published regarding a former American professional football player who had progressive cognitive, behavioral, and mood problems during life, as well as neuropathological evidence of CTE after death. <sup>9</sup>
<b>2013</b>	CTE is described neuropathologically in 68 individuals whose brains had been donated to research and who had a history of repetitive head impact exposure, including military veterans and athletes who had played professional and amateur contact sports (e.g., American football, boxing, rugby, soccer). <sup>10</sup>
<b>2013–2014</b>	The clinical presentation of CTE is described, and provisional research diagnostic criteria for traumatic encephalopathy syndrome is proposed. <sup>10–12</sup>
<b>2015</b>	The first National Institutes of Health (NIH) Consensus Workshop to Define the Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy is held. <sup>10</sup>

## Clinical Presentation

Some research, based on a postmortem CTE determination, suggests that the signs and symptoms of CTE present years or decades after the period in which repetitive head impacts were experienced. The age of symptom onset varies from as early as 19 years of age to over 65 years of age.<sup>10,12,13</sup>

Descriptions of the clinical features of CTE are based primarily on interviews with family members of deceased individuals who were diagnosed with CTE after death.<sup>10,12,13</sup> Therefore, there is a need for more research, including longitudinal studies, to better understand the clinical presentation of CTE and to explore the pathological correlation.<sup>3</sup>

CTE symptoms are believed to fall into two initial clinical presentations that are associated with the age of symptom onset:<sup>12,14</sup>

- **Younger age** (average age 35): Symptom onset is associated with mood and behavioral impairments, often with cognitive deficits occurring later in the course of the disease.
- **Older age** (average age 60): Symptom onset is associated with cognitive deficits. Many will present with a combination of cognitive, mood, and behavioral symptoms throughout the course of the disease. The majority of individuals with advanced stage CTE experience worsening of their cognitive deficits, resulting in impaired daily functioning and dementia. Often, these individuals have clinical presentations similar to patients with Alzheimer’s disease dementia, although neuropathological examinations demonstrate no evidence of Alzheimer’s pathology.

### Signs and Symptoms Generally Fall Into Four Groups



**COGNITIVE:** Problems with memory, executive functioning, and impaired attention.



**BEHAVIORAL:** Impulsivity, quick temper (“short fuse”), verbal and physical violence, and rage.



**MOOD:** Depression, hopelessness, anxiety, and apathy.



**MOTOR:** Parkinsonism, including ataxia, dysarthria, poor gait, tremor, and masked facies.

## Risk Factors

Individuals may have a higher risk of developing CTE in the future if they engage in activities that increase their chances of having repetitive hits to the head.

Researchers currently do not know the incidence and prevalence of CTE, but they do know that CTE does not occur only in athletes. The greatest risk factor for CTE is the number of years of exposure to repeated head or brain injuries (subconcussions in particular).<sup>13</sup> However, it is not yet known how many repeated head or brain injuries increase the risk for CTE. Not everyone who has repeated head or brain injuries will get CTE, and there is no evidence that one concussion will lead to CTE. Research on the role of genetics, comorbid medical conditions, sex, and other factors is needed to better understand the risk factors for CTE.

## Diagnosis

At this time, a diagnosis of CTE can only be confirmed through postmortem neuropathological examination. The pathognomonic lesion of CTE involves an irregular deposition of p-tau around small blood vessels at the base of the cortical sulci.<sup>13</sup> At the NIH Consensus Workshop to Define the Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy,<sup>15</sup> this pattern of p-tau was agreed to be distinct from any other neurodegenerative tauopathy, including Alzheimer's disease and frontotemporal lobar degeneration.

Currently, CTE cannot be diagnosed during life. Provisional research diagnostic criteria for the clinical manifestation of CTE, referred to as traumatic encephalopathy syndrome (TES), have been proposed.<sup>11</sup> However, at this time, there are no validated biomarkers for CTE, and the reliability and validity of the provisional research diagnostic criteria for TES (or similar proposed "clinical criteria"<sup>16</sup>) have not been reported. Therefore, it is premature for practicing healthcare providers to implement TES as a diagnostic entity. Similarly, it is premature for patients to be informed that they likely have CTE based on the results of experimental, nonvalidated procedures that are not yet approved by the Food and Drug Administration.

## Advancing Research on CTE



In 2013, NIH launched a major program to advance research to better understand CTE, its causes, and how to diagnose it while a person is alive. To learn more, visit the [National Institute of Neurological Disorders and Stroke \(NINDS\) Traumatic Brain Injury Information page](#).

To read a report from the Consensus Meeting on CTE Neuropathology hosted by NIH, go to the [Report from the First NIH Consensus Workshop to Define the Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy](#).

## Improving Diagnosis of CTE



To fill current gaps in knowledge about the disease, researchers are studying methods to diagnose CTE during life, including through the use of experimental PET scans, MRI scans, tests of cerebrospinal fluid, and even blood tests. As part of this effort, a large research study funded by NIH is currently underway.<sup>3</sup> In 2015, NINDS funded a \$16M, 7-year, multi-center grant known as [DIAGNOSE CTE](#) (Diagnostics, Imaging, and Genetics Network for the Objective Study and Evaluation of Chronic Traumatic Encephalopathy).

## Talking With Patients About CTE



Growing awareness of CTE has led to an increasing number of patients and caregivers who are concerned about the disease. Without available methods to diagnose CTE during life, healthcare providers can educate patients about CTE (see CDC's "Answering Questions About Chronic Traumatic Encephalopathy" handout).

- **For younger individuals** with mood and behavioral impairments consistent with CTE, it is important to understand that:
  - These symptoms can be experienced by people who do not have CTE or who have never been exposed to repetitive head impacts, and such symptoms may represent idiopathic disorders.<sup>17</sup>
  - Treatment of symptoms should coincide with appropriate emotional or behavior supports.
  - CTE cannot be diagnosed during life, and much more research on the disease is needed.

- **For older individuals** with a history of extensive repetitive head impact exposure and progressive memory and other cognitive impairments, CTE could be included in the differential diagnosis. If amyloid PET imaging is available and the results are negative, the possibility that CTE is the underlying cause of the symptoms is strengthened (i.e., Alzheimer's disease would be less likely), although the evidence is still not conclusive. At this time, healthcare providers may benefit from:
  - Awareness of CTE and the possibility that some patients, especially those with extensive exposure to repetitive head impacts, may be suffering from it.
  - An understanding that CTE cannot yet be diagnosed during life.
  - Provision of appropriate symptomatic treatment.
  - Awareness that much more research is needed.

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