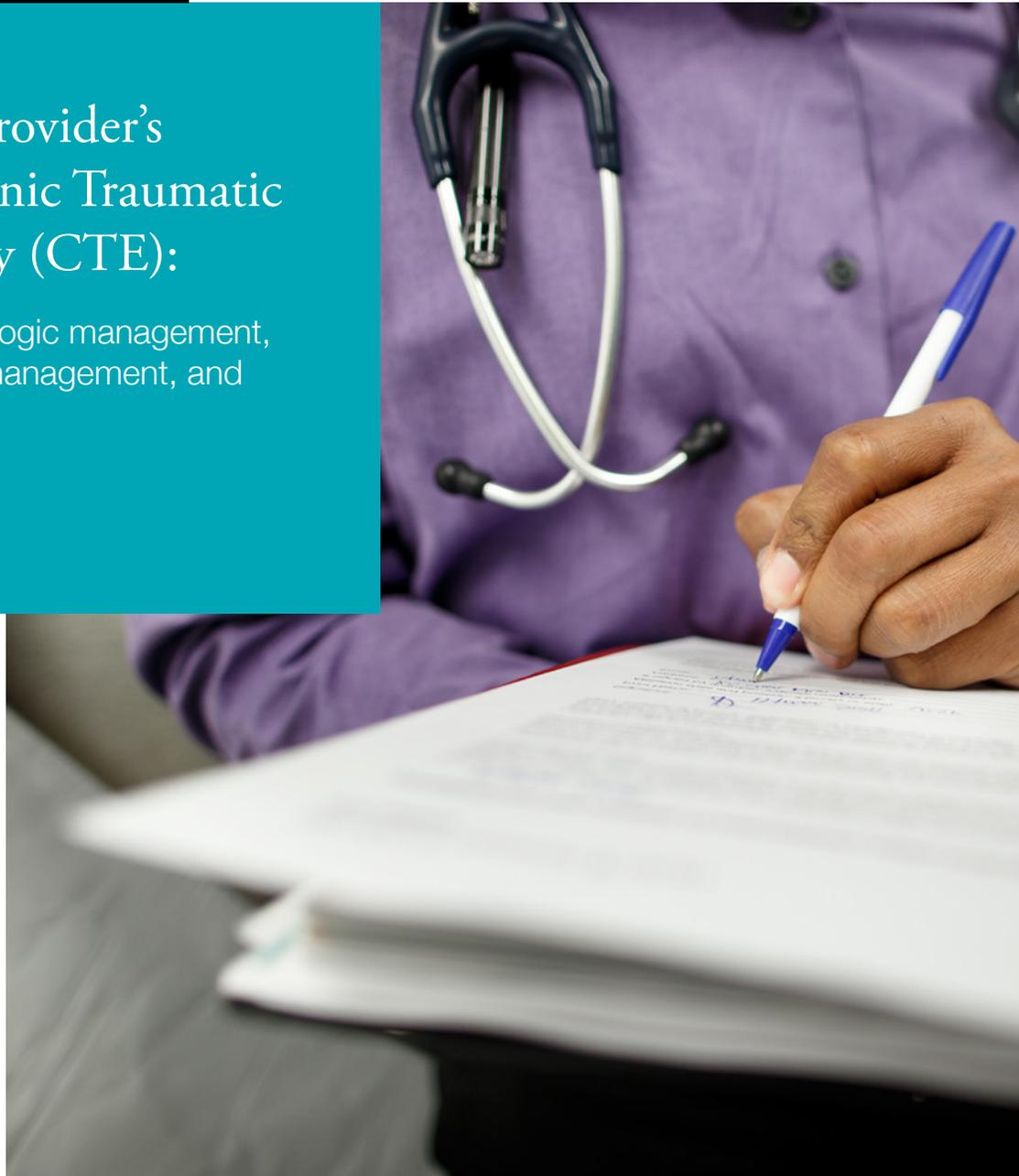


A Healthcare Provider's Guide To Chronic Traumatic Encephalopathy (CTE):

Diagnosis, pharmacologic management,
non-pharmacologic management, and
other considerations

This material is provided
by UCSF Weill Institute
for Neurosciences as an
educational resource for
health care providers.





A Healthcare Provider's Guide To Chronic Traumatic Encephalopathy (CTE): Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

Diagnosis

Definition

Dementia is a clinical syndrome defined as a cognitive or behavioral decline that leads to an inability to complete daily tasks independently. Dementia has many causes some of which are reversible, such as metabolic disorders, while some are progressive such as Alzheimer disease and behavioral variant frontotemporal dementia (bvFTD).

Chronic traumatic encephalopathy (CTE) is a degenerative brain disease that can lead to dementia symptoms and is seen in some people who have had multiple concussions or multiple traumatic impacts to the head. Despite increased media coverage of CTE in veterans and professional athletes, there is no accepted consensus description of CTE yet, and risk factors for developing it are not certain but likely include the number, mechanics, severity, and timing of traumatic brain injuries (TBIs), genetics, and other lifestyle and environmental factors. CTE is characterized by a unique pathological distribution of tau deposits¹, and a wide range of behavioral, cognitive, and motor changes including depression, aggression, memory loss, loss of attention, and parkinsonism.

Etiology

While TBI does not lead to CTE in every person with head injury, it appears to be a necessary trigger to develop it. However, a deeper understanding of the TBI risk is needed: how many, how severe, location, how long ago, etc. Currently diagnosis is

made at autopsy, which has an inherent selection bias, so good estimates of prevalence in the population do not exist, nor do clear characterizations of the people affected by CTE beyond selected athletes and veterans.

Course

Symptoms associated with stage¹ (the mildest pathology) include headaches and inattention; symptoms associated with stage² include mood changes, explosive reactions, and memory impairment. Patients with stage³ pathology show more cognitive impairment, particularly executive dysfunction. Patients with stage⁴ pathology are more likely to have a dementia diagnosis, show aggression, and have word finding difficulty. Progression tends to be slower than in other neurodegenerative illnesses.²

Differential Diagnosis

CTE is often mistaken for Alzheimer's disease, frontotemporal dementia, mood and psychotic disorders, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). In some patient, CTE can coexist with other neurodegenerative pathologies such as Alzheimer's disease.

Diagnostic Criteria

No consensus has been reached on appropriate clinical diagnostic criteria for CTE. Better understanding of disease risk, presentation, and progression is needed. Jordan proposed these criteria in 2013.³

Classification	Definition	Clinical Examples
Definite	Any neurological process consistent with the clinical presentation of CTE along with pathological confirmation (tauopathy ± diffuse amyloid deposition ± TDP-43 deposition)	Cognitive, behavioral, and/or motor dysfunction
Probable	Any neurological process characterized by two or more of the following conditions: cognitive and/or behavioral impairment; cerebellar dysfunction; pyramidal tract disease or extrapyramidal disease; clinically distinguishable from any known disease process and consistent with the clinical description of CTE	Cognitive impairment and extrapyramidal dysfunction suggestive of parkinsonism Associated cerebellar dysfunction that is inconsistent with parkinsonism
Possible	Any neurological process that is consistent with the clinical description of CTE but can be potentially explained by other known neurological disorders	Alzheimer disease or other primary dementia Parkinson disease Primary cerebellar degeneration Wernicke–Korsakoff syndrome Amyotrophic lateral sclerosis
Improbable	Any neurological process that is inconsistent with the clinical description of CTE and can be explained by a pathophysiological process unrelated to brain trauma	Cerebrovascular disease Multiple sclerosis Brain neoplasm Other inherited neurological disorders

Pharmacologic Management

Medications to Use

There are several classes of medications used to treat disease symptoms or improve cognitive function. Selective serotonin reuptake inhibitors (SSRIs), atypical antipsychotics, and cholinesterase inhibitors may be helpful for managing different behavioral and cognitive problems. Currently, there are no disease-modifying treatments for CTE. Small open labels studies have demonstrated a potential humble effect for cholinesterase inhibitors in helping the cognitive symptoms of traumatic brain injury.

Review expected and realistic goals of treatment (e.g., treatment is for symptomatic improvement and not a cure or reversal of disease). Expected benefits may be mild improvement in memory function, mood, and alertness. If the patient has vascular disease or mixed dementia, they should receive management and education regarding modification of cardiovascular risk factors.

Medications to Avoid

Medications with strong anticholinergic side effects, such as sedating antihistamines, barbiturates, narcotics, benzodiazepines, gastrointestinal and urinary antispasmodics, central nervous system (CNS) stimulants, muscle relaxants, and tricyclic antidepressants should be avoided. Antipsychotics should be used with caution. If used, carefully evaluate effectiveness of medication and consider discontinuing if there is no improvement in six weeks.^{4,5,6}

Non Pharmacologic Management

Healthy Lifestyle

There are lifestyle habits that promote health and well-being. Research suggests that the combination of good nutrition, physical activity, and mental and social engagement may provide benefit in promoting health although more study is needed to determine the actual mechanisms.^{7,8} A heart-healthy diet (lower in sugar and fat and higher in vegetables and fruit) is considered to be good for both the body and the brain. An example is the Mediterranean diet that promotes nutrition based on fruit, vegetables, nuts, and grains with limits on consumption of red meat and saturated fats. Physical exercise has been associated with improvement of mood and mobility, and a decrease in the risk for falls.^{9,10} Physical activities that are socially engaging (walking or swimming with a friend and participating in exercise groups) can be especially enjoyable. Engagement in activities that are mentally stimulating (crossword puzzles, sudoku, computer games) is encouraged as long as the activity is enjoyable.

The Alzheimer's Association has more information on tips for maintaining your health: alz.org/we_can_help_brain_health_maintain_your_brain.asp.

Sleep

Disrupted sleep can negatively impact memory and thinking, though the mechanisms are not well understood.¹¹

Components of sleep hygiene include:

- Avoid napping during the day
- Avoid stimulants such as caffeine, nicotine, and alcohol too close to bedtime
- Get regular exercise
- Avoid eating right before sleep
- Ensure adequate exposure to natural light
- Establish a regular relaxing bedtime routine
- Associate your bed with sleep. It's not a good idea to use your bed to watch TV, listen to the radio, or read.

For more details on sleep hygiene, you can refer to the National Sleep Foundation at sleepfoundation.org/ask-the-expert/sleep-hygiene.

Other Considerations

Support Resources

- Patrick Risha CTE Awareness Foundation: stopcte.org
- Brain Injury Association of America (BIAA): biausa.org
- Alzheimer's Association: alz.org
- Family Caregiver Alliance: caregiver.org
- National Institute of Health/National Institute on Aging: nia.nih.gov/alzheimers
- The Association for Frontotemporal Degeneration: theaftd.org/

Research and Clinical Trials

The National Institutes of Health maintains an extensive listing of clinical trials at clinicaltrials.gov. Academic medical centers may be engaged in research and clinical trials.

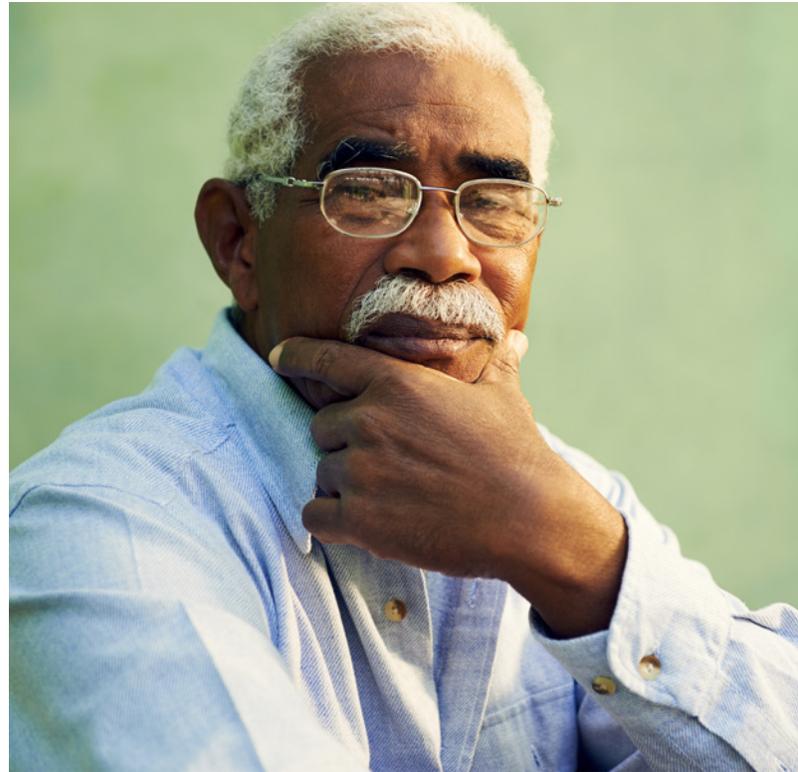
Safety

If wandering or getting lost is a concern, refer the patient and family to the MedicAlert +Alzheimer's Association Safe Return program (operated by the Alzheimer's Association) alz.org/care/dementia-medic-alert-safe-return.asp.

Other strategies for ensuring safety concerns may include door alarms and increased supervision.

Driving

Depending on cognitive and motor findings, the patient may be requested to stop driving, complete test of driving abilities through the Department of Motor Vehicles (DMV), or be referred to a driver's safety course that will assess driving ability. Reporting to the DMV should be consistent with state laws. Some states have mandatory reporting requirements: the diagnosis is reported to local health departments who then report to the DMV. Individual state requirements can be found at: dmvusa.com.



Living Situation and Environment

It is important to determine if the patient's residential setting best meets his or her functional and cognitive abilities. Areas of concern may include personal safety (ability to manage medications safely, ability to manage nutritional requirements, ability to manage personal hygiene) and quality of life (activities and engagement that match the person's needs and abilities).

Types of living situations range from living at home alone or living at home with supervision, to board and care, assisted living, or memory care units.

Elder Abuse

Patients with dementia and their caregivers are vulnerable to abuse. Refer to Adult Protective Services (APS) if there is concern for the well-being of the patient or the caregiver.

To locate an APS office in your state, see: napsa-now.org/get-help/help-in-your-area/.

Legal Planning

Provide information about advance directives and durable power of attorney while the patient is in the early stages of disease and able to articulate his or her wishes. Make referrals for legal and financial advice, especially if there are concerns about the patient's judgment, decision-making, or vulnerability. A formal evaluation for capacity may be warranted. The Alzheimer's Association provides a brochure that covers legal planning: alz.org/national/documents/brochure_legalplans.pdf.



• **Advanced Directives**

These documents allow individuals to state their preferences for medical treatments and to select an agent or person to make health care decisions in the event they are unable to do so or if they want someone else to make decisions for them.

• **Power Of Attorney**

A Power of Attorney (POA) is a legal document that gives someone of an individual's choosing the power to act in their place. POAs can be for medical or financial matters.

• **Living Will**

A living will is a written, legal document that spells out medical treatments that an individual would and would not want to be used to keep them alive, as well as other decisions such as pain management or organ donation.

Teaching Video for Providers

An example of a physician telling a patient she has dementia: alz.org/health-care-professionals/dementia-diagnosis-diagnostic-tests.asp#alzheimers_diagnosis.



References

1. Corsellis JAN, Bruton CJ, Freeman-Browne D. The aftermath of boxing1. *Psychological Medicine*. 1973;3(03):270. 2. Schoen FJ. Cardiac pathology in asthma. *Journal of Allergy and Clinical Immunology*. 1987;80(3):419-423. 3. Jordan BD. The clinical spectrum of sport-related traumatic brain injury. *Nature Reviews Neurology*. 2013;9(4):222-230. 4. Han L, Mccusker J, Cole M, Abrahamowicz M, Primeau F, Élie M. Use of Medications With Anticholinergic Effect Predicts Clinical Severity of Delirium Symptoms in Older Medical Inpatients. *Archives of Internal Medicine*. 2001;161(8):1099. 5. Roe CM, Anderson MJ, Spivack B. Use of Anticholinergic Medications by Older Adults with Dementia. *Journal of the American Geriatrics Society*. 2002;50(5):836-842. 6. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society*. 2012;60(4):616-631. 7. Barnes DE, Santos-Modesitt W, Poelke G, et al. The Mental Activity and eXercise (MAX) Trial. *JAMA Internal Medicine*. 2013;173(9):797. 8. Jedrziowski MK, Ewbank DC, Wang H, Trojanowski JQ. The Impact of Exercise, Cognitive Activities, and Socialization on Cognitive Function. *American Journal of Alzheimer's Disease & Other Dementias*®. 2014;29(4):372-378. 9. Howe TE, Rochester L, Neil F, Skelton DA, Ballinger C. Exercise for improving balance in older people. *Cochrane Database of Systematic Reviews*. September 2011. 10. Podewils LJ. Physical Activity, APOE Genotype, and Dementia Risk: Findings from the Cardiovascular Health Cognition Study. *American Journal of Epidemiology*. 2005;161(7):639-651. 11. Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. *The Lancet Neurology*. 2014;13(10):1017-1028.