Test Definition: RTQPC

Abnormal Prion Protein, Real-Time Quaking Induced Conversion, Spinal Fluid (Non-Orderable)

Overview

Useful For

Only orderable as part of a profile. For more information see:
CJDE / Creutzfeldt-Jakob Disease Evaluation, Spinal Fluid
RPDE / Rapidly Progressive Dementia Evaluation, Spinal Fluid

Aiding in diagnosing sporadic Creutzfeldt-Jakob disease or other prion disease in patients with a rapidly progressive dementia

Method Name

Only orderable as part of a profile. For more information see:
CJDE / Creutzfeldt-Jakob Disease Evaluation, Spinal Fluid
RPDE / Rapidly Progressive Dementia Evaluation, Spinal Fluid

Real-Time Quaking-Induced Conversion (RT-QuIC)

NY State Available

Yes

Specimen

Specimen Type

CSF

Specimen Required

Only orderable as part of a profile. For more information see:
CJDE / Creutzfeldt-Jakob Disease Evaluation, Spinal Fluid
RPDE / Rapidly Progressive Dementia Evaluation, Spinal Fluid

Specimen Minimum Volume

See Specimen Required

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Discolored CSF	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	28 days	BlueTop SARSTEDT
	Ambient	12 hours	BlueTop SARSTEDT
	Refrigerated	14 days	BlueTop SARSTEDT

Clinical & Interpretive

Clinical Information

This evaluation is intended for use in patients with suspected Creutzfeldt-Jakob disease (CJD) and other human prion diseases. CJD is a rare and fatal neurodegenerative disorder that predominantly affects the brain and is caused by misfolded prion proteins (PrP[Sc]). CJD accounts for more than 90% of human prion diseases. Initial symptom onset is heterogenous but commonly includes rapidly progressive dementia, cerebellar ataxia, and myoclonus. The timeline of symptom progression and the pattern of symptom evolution can be divergent across patients and CJD subtypes, making an accurate diagnosis based on clinical presentation alone challenging. The inclusion of biomarkers with high diagnostic accuracy has improved the differentiation of CJD and related prion diseases from treatable neurological conditions with overlapping phenotypes. The real-time quaking-induced conversion (RT-QuIC) assay has been established to have strong clinical utility for early and accurate diagnosis of CJD through numerous independent studies in cerebrospinal fluid (CSF). Furthermore, the robustness and reproducibility of the RT-QuIC assay for CJD across laboratories has been demonstrated through international ring trials. The clinical sensitivity and specificity of second-generation RT-QuIC assays in CSF have been consistently reported to be greater than or equal to 92% and greater than or equal to 99%, respectively. Despite the high diagnostic accuracy of the assay, RT-QuIC results should be interpreted in the appropriate clinical context along with other clinical and paraclinical findings. A definitive diagnosis of sporadic prion disease can be established only through neuropathological assessment of brain tissue.

Unexpectedly negative RT-QuIC test results should prompt careful consideration of the differential diagnosis. If there is high suspicion of prion disease, repeat testing with RT-QuIC may be warranted. A small subset of cases initially negative by RT-QuIC may become positive as the disease progresses. However, RT-QuIC may be persistently negative in a small proportion of patients with definitive prion disease. False-negative RT-QuIC results are most often encountered in cases of genetic prion disease (eg, fatal familial insomnia and Gerstmann-Straussler-Scheinker disease) and in atypical sporadic prion disease subtypes (eg, MM2 cortical subtype) that have slower indolent disease progression. Other CSF biomarkers have been utilized to support the diagnosis of CJD, including 14-3-3, total Tau measurement, and the ratio of total Tau to phosphorylated Tau at threonine 181. Recent studies have indicated that the Tau ratio (total Tau to pT181-Tau or vice versa) has a very high diagnostic accuracy that exceeds that provided by total Tau or 14-3-3 enzyme-linked immunosorbent assays (ELISA). In a cohort of probable/definite CJD cases and controls tested utilizing the Roche Total-Tau and p-Tau (threonine 181) Elecsys assays, the optimized cut-off value for total Tau (>393 ng/L) had a clinical sensitivity and specificity of 92.3% and 88.3% for CJD, respectively, and the optimized cut-off value for the total Tau to p-Tau ratio (>18) has a clinical sensitivity and specificity of 97.4% and 95.9% for CJD, respectively.

Importantly, total Tau or total Tau to p-Tau ratios utilize assay-dependent cut-off values, and cut-off values from one assay are not transferable to different assay platforms.

The National Prion Disease Pathology Surveillance Center (NPDPSC) coordinates autopsies and neuropathologic examinations on suspected prion disease cases. More information about services available at the NPDPSC can be found at https://case.edu/medicine/pathology/divisions/prion-center.

Reference Values

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CJDE / Creutzfeldt-Jakob Disease Evaluation, Spinal Fluid
RPDE / Rapidly Progressive Dementia Evaluation, Spinal Fluid

Negative

Interpretation

A positive real-time quaking-induced conversion (RT-QuIC) assay result is supportive of prion disease and, in the correct clinical context, fulfills the Centers of Disease Control and Prevention diagnostic criteria of probable prion disease.(1)

Negative results do not exclude the possibility of prion disease.

Cautions

These test results should be interpreted in the appropriate clinical context along with other clinical and paraclinical findings. Only through neuropathological assessment of brain tissue can a definitive diagnosis of sporadic prion disease be established.

Some molecular subtypes of prion protein have been reported to have lower detectability by real-time quaking-induced conversion (RT-QuIC).

Even small quantities of blood in CSF can result in false-negative RT-QuIC results.
The presence of fluorescent substances may interfere with testing and prevent an accurate interpretation of the RT-QuIC assay.

Careful consideration of the differential diagnosis is advised when RT-QuIC test results are unexpectedly negative. Repeat testing with RT-QuIC may be warranted if there is high suspicion of prion disease. A small subset of initially negative cases by RT-QuIC may become positive as the disease progresses. However, a small proportion of patients with definitive prion disease may be persistently negative by RT-QuIC. False-negative RT-QuIC results are most often encountered in cases of genetic prion disease, such as fatal familial insomnia and Gerstmann-Straussler-Scheinker disease, and in atypical sporadic prion disease subtypes that have slower indolent disease progression.

Clinical Reference

1. Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP). Diagnostic criteria: CDC's diagnostic criteria for Creutzfeldt-Jakob disease (CJD), 2018. CDC; Updated October 18, 2021. Accessed July 17, 2024. Available at

www.cdc.gov/creutzfeldt-jakob/hcp/clinical-overview/diagnosis.html
2. Hermann P, Appleby B, Brandel JP, et al. Biomarkers and diagnostic guidelines for sporadic Creutzfeldt-Jakob disease. Lancet Neurol. 2021;20(3):235-46
3. Rhoads DD, Wrona A, Foutz A, et al. Diagnosis of prion diseases by RT-QuIC results in improved surveillance. Neurology. 2020;95(8):e1017-e1026
4. Hamlin C, Puoti G, Berri S, et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. Neurology. 2012;79(6):547-552
5. Shir D, Lazar EB, Graff-Radford J, et al. Analysis of clinical features, diagnostic tests, and biomarkers in patients with suspected Creutzfeldt-Jakob disease, 2014-2021. JAMA Netw Open. 2022;5(8):e2225098

Performance

Method Description

This assay is a second-generation seeding aggregation assay known as a real-time quaking-induced conversion assay (RT-QuIC). Briefly, the cerebrospinal fluid sample is mixed with reaction buffer that contains fluorescence emitting dye and truncated recombinant hamster prion proteins (amino acids 90-231) in a 96-well black microtiter plate with clear optical bottom. Each 96-well plate includes 2 positive controls and 2 negative controls plus 20 samples. Each sample is tested in 4 replicate wells. At completion of the reaction, if at least one of the reaction wells per sample is scored positive, testing is repeated for that sample. The assay is performed on a BMG Omega FLUOStar instrument.(Orru CD, Groveman BR, Hughson AG, et al. RT-QuIC assays for prion disease detection and diagnostics. Methods Mol Biol. 2017;1658:185-203)

PDF Report

No

Day(s) Performed

Monday, Tuesday, Thursday, Sunday

Report Available

3 to 8 days

Specimen Retention Time

60 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

0584U

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
RTQPC	RT-QuIC Prion, CSF	No LOINC Needed

Result ID	Test Result Name	Result LOINC® Value
620307	RT-QuIC Prion, CSF	101662-5