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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи.** Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html. В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე, დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემავჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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SPORADIC CREUTZFELDT–JAKOB DISEASE: CLINICAL FEATURES, DIAGNOSIS AND THERAPEUTIC HORIZONS

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Abstract.

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare, rapidly progressive, and fatal prion disease that remains a major diagnostic and therapeutic challenge. Its presentation often overlaps with other causes of rapidly progressive dementia, making early recognition essential, particularly to exclude potentially reversible conditions. This review provides an updated overview of the diagnostic tools, cerebrospinal fluid (CSF) biomarkers, prognostic factors, clinical progression, differential diagnosis, and current management strategies in sCJD. A literature-based review was conducted using PubMed and Scopus for articles published between October 1, 2015, and October 1, 2025, focusing on patients with suspected or confirmed CJD. Clinical features, magnetic resonance imaging (MRI), electroencephalography (EEG), CSF biomarkers, prognostic indicators, and therapeutic approaches were synthesized. Current diagnosis of sCJD relies on the integration of clinical presentation with MRI, EEG, and CSF testing. Diffusion-weighted MRI and real-time quaking-induced conversion (RT-QuIC) have substantially improved antemortem diagnostic accuracy, while traditional biomarkers such as 14-3-3 protein and total tau remain useful supportive tests. Prognosis is uniformly poor, with median survival usually limited to a few months, although disease course varies according to age, PRNP codon 129 polymorphism, and molecular subtype. Important differential diagnoses include autoimmune encephalitis, viral encephalitis, vascular cognitive impairment, and other neurodegenerative disorders presenting with rapidly progressive dementia. No disease-modifying therapy has shown definitive benefit, and management remains primarily supportive and symptom-directed. Advances in biomarkers and greater understanding of molecular heterogeneity may improve early diagnosis, prognostication, and future therapeutic development.

Key words. Sporadic Creutzfeldt-Jakob disease, prion disease, rapidly progressive dementia, neurodegeneration.

Introduction.

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare, fatal neurodegenerative disorder caused by the misfolding of prion proteins in the central nervous system. It is the most common form of human prion disease, with an annual incidence of approximately 1-2 cases per million individuals [1]. Clinically, sCJD typically manifests as a rapidly progressive dementia accompanied by a variety of neurological signs, ultimately leading to death within months of symptom onset [2]. Key challenges in the management of sCJD include early and accurate diagnosis - particularly to differentiate it from treatable causes of rapidly progressive dementia - prognostication due to its heterogeneous clinical course, and the absence of effective disease-modifying therapies. This narrative review summarizes

current evidence on diagnostic criteria and tools, including recent advances in magnetic resonance imaging (MRI), electroencephalography (EEG), and cerebrospinal fluid (CSF) biomarkers. It also discusses prognostic indicators, clinical subtypes, emerging therapeutic approaches, and the differential diagnosis of rapidly progressive dementia in patients with suspected CJD.

Scope of the Review and Literature Selection.

This article was designed as a narrative review rather than a systematic review or meta-analysis. The aim was to provide a clinically oriented synthesis of recent evidence on sporadic Creutzfeldt-Jakob disease, with emphasis on clinical presentation, diagnostic tools, differential diagnosis, prognostic factors, disease progression, and current or emerging therapeutic strategies.

A structured literature search was performed in PubMed/MEDLINE and Scopus for articles published between October 1, 2015, and October 1, 2025. Search terms included combinations of "sporadic Creutzfeldt-Jakob disease," "CJD," "prion disease," "rapidly progressive dementia," "MRI," "diffusion-weighted imaging," "EEG," "14-3-3," "total tau," "RT-QuIC," "prognosis," "survival," "molecular subtype," and "treatment." Additional older landmark studies were included when necessary to provide historical context or describe established diagnostic criteria and molecular classification.

After removal of duplicates, 225 records were screened by title and abstract. Articles were considered eligible if they addressed suspected or confirmed CJD and provided relevant information on clinical features, diagnostic accuracy, CSF biomarkers, neuroimaging, EEG, prognosis, differential diagnosis, surveillance, or therapeutic approaches. Articles were excluded if they were duplicates, unrelated to human CJD, outside the objectives of the review, unavailable in English, conference abstracts without sufficient detail, or lacked clinically relevant data. Based on these criteria, 109 articles were selected for full-text review and used to inform the narrative synthesis.

Because of the heterogeneity of study designs, diagnostic definitions, patient populations, outcomes, and reporting methods, no meta-analysis or formal risk-of-bias assessment was performed.

Discussion.

Diagnostic Tools and Criteria in sCJD:

Accurate diagnosis of sporadic Creutzfeldt-Jakob disease (sCJD) has significantly improved with modern diagnostic tools. A definitive diagnosis still requires neuropathological confirmation - via brain biopsy or autopsy demonstrating prion protein aggregates [3]. However, in clinical practice, sCJD can be diagnosed with high confidence using clinical criteria in

combination with MRI and cerebrospinal fluid (CSF) biomarkers [3]. In 2017, international consensus criteria for sCJD were revised to incorporate advanced diagnostic tests - most notably diffusion-weighted MRI and the real-time quaking-induced conversion (RT-QuIC) assay - as major criteria for "probable" CJD [4-6]. The typical clinical picture includes rapidly progressive cognitive decline with at least two of the following four features: myoclonus, visual or cerebellar disturbance, pyramidal/extrapyramidal signs, or akinetic mutism, and no alternative explanation [7,8]. A diagnosis of probable sCJD can then be established in the appropriate clinical context by the presence of one or more of the following: characteristic MRI findings (e.g., high signal in caudate/putamen or cortical ribboning), periodic EEG, elevated CSF 14-3-3 protein, or a positive RT-QuIC result [6,9].

MRI and Neuroimaging:

Magnetic resonance imaging (MRI) of the brain - particularly diffusion-weighted imaging (DWI) - is a cornerstone of sCJD diagnosis. DWI often reveals hyperintense signal abnormalities in the cortical ribbon and deep nuclei early in the disease, reflecting diffusion restriction caused by spongiform change and gliosis (Figure 1) [9]. Classic MRI signs in prion disease include cortical ribboning (bright DWI signal in the cortex) and hyperintensity of the basal ganglia; in variant CJD, the "pulvinar sign" (signal in the thalamic pulvinar nucleus) is characteristic, though thalamic involvement - including the so-called "hockey stick" sign in the medial thalamus - can occasionally appear in advanced sCJD as well [10]. These changes are often bilateral but may be asymmetric [11]. Initially, MRI changes can be subtle, but they become more pronounced as the disease progresses alongside rapidly evolving brain atrophy [12]. Notably, by incorporating DWI/FLAIR hyperintensities in specific regions (caudate/putamen or at least two cortical lobes) into diagnostic criteria, MRI now yields high sensitivity and specificity for sCJD [3,5]. Overall, typical MRI changes are observed in approximately 70-95% of sCJD patients (depending on reader expertise and criteria) and have ~98% specificity for sCJD when the appropriate distribution of lesions is seen [3,13,14].

Emerging neuroimaging techniques are being investigated as adjuncts to conventional MRI in the evaluation of CJD. Fluorodeoxyglucose positron emission tomography (FDG-PET) frequently demonstrates cortical and deep gray matter hypometabolism corresponding to regions affected by prion pathology and may provide clues to disease subtype, although it cannot reliably differentiate sporadic from genetic CJD [15]. Single-photon emission computed tomography (SPECT) can similarly reveal focal perfusion deficits that often parallel diffusion-weighted imaging (DWI) abnormalities [15]. While these functional imaging modalities are not incorporated into standard diagnostic criteria, they may offer supportive evidence in atypical or diagnostically challenging cases [16]. Beyond confirming prion disease, neuroimaging plays a critical role in excluding alternative causes of rapidly progressive dementia. For example, MRI can identify structural conditions such as normal pressure hydrocephalus, CNS vasculitis, or intracranial tumors, while autoimmune encephalitis typically exhibits limbic T2 hyperintensities with contrast enhancement - features absent

in CJD [17,18]. Thus, MRI remains indispensable not only for establishing a probable CJD diagnosis but also for differentiating it from other treatable etiologies of rapid neurological decline.

Electroencephalography:

Electroencephalography (EEG) was among the earliest diagnostic tools for CJD. As the disease advances, approximately two-thirds of patients develop a characteristic periodic pattern consisting of generalized, synchronous bi- or triphasic sharp-wave complexes at about 1 Hz [19]. These periodic sharp wave complexes (PSWCs) were incorporated into older WHO criteria for probable CJD and, when present, are highly suggestive of the diagnosis [20]. Typically, PSWCs emerge during the mid-stage of illness - often weeks after symptom onset - and may disappear in late-stage sCJD as cortical activity declines markedly [19]. Despite their diagnostic value, EEG findings are not universally present. The sensitivity of EEG for sCJD is approximately 64-67%, with specificity ranging from ~74-94% [21]. This means that while a positive EEG pattern strongly supports the diagnosis, a substantial proportion of patients never exhibit the classic changes. Consequently, EEG is now considered an ancillary test rather than a primary criterion in modern diagnostic frameworks. It is important to recognize that EEG may be normal or show only nonspecific diffuse slowing in the early stages of sCJD (19). Rarely, nonconvulsive status epilepticus can mimic CJD both clinically and on EEG; in such cases, responsiveness to antiepileptic therapy is a key distinguishing feature [22]. Overall, while the presence of periodic sharp wave complexes strongly supports a diagnosis of sCJD, a normal EEG does not exclude the disease. Modern MRI and CSF-based assays have largely supplanted EEG in diagnostic weight, yet EEG remains a valuable adjunct - particularly when MRI or CSF findings are equivocal.

Cerebrospinal Fluid Biomarkers:

Because brain biopsy is invasive, cerebrospinal fluid (CSF) biomarkers are central for establishing a biological diagnosis of Creutzfeldt-Jakob disease (CJD) *in vivo*. Classic markers for sporadic CJD (sCJD) include 14-3-3 protein and total tau, which rise due to rapid prion-related neurodegeneration. More recently, prion seed amplification assays such as real-time quaking-induced conversion (RT-QuIC) have transformed diagnostics by directly detecting misfolded prion protein activity with high specificity.

RT-QuIC: Real-time quaking-induced conversion is a prion seed amplification assay that detects disease-associated prion seeding activity. Compared with surrogate neuronal injury markers such as 14-3-3 protein and total tau, RT-QuIC has substantially higher specificity because it directly reflects prion seeding activity rather than nonspecific neuronal damage. A positive CSF RT-QuIC result in the appropriate clinical context strongly supports probable CJD, whereas a negative result does not fully exclude the diagnosis, particularly in atypical molecular subtypes or very early disease. RT-QuIC has therefore become central to modern diagnostic criteria and has reduced reliance on invasive brain biopsy.

In addition to CSF-based RT-QuIC, RT-QuIC testing using olfactory mucosa samples obtained by nasal brushing has been explored as a promising minimally invasive diagnostic

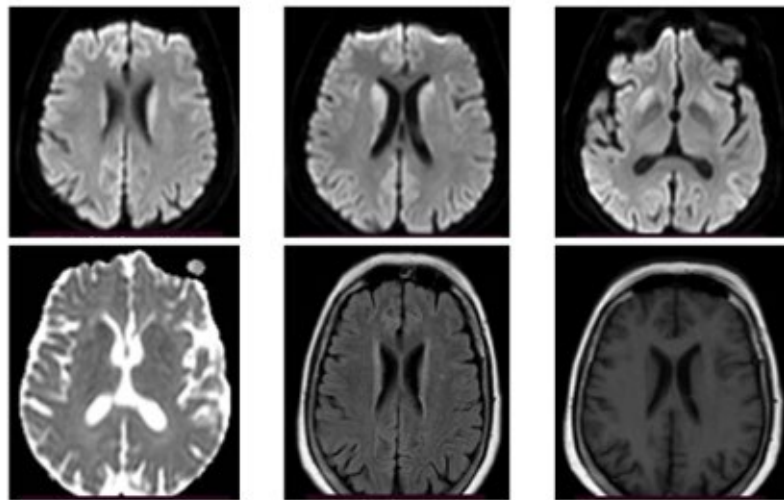


Figure 1. Diffusion-weighted MRI findings reported in patients with sporadic CJD, showing ribbon-like cortical hyperintensity along the gyri and signal elevation in the basal ganglia. Restricted diffusion reflects spongiform change. FLAIR sequences typically reveal corresponding abnormalities, though often less prominently than DWI in early disease.



Figure 2. Electroencephalogram (EEG) findings reported in patients with sporadic sCJD. The EEG demonstrates diffuse background slowing with generalized, synchronous periodic sharp-wave complexes (PSWCs) occurring at approximately 1 Hz. These complexes, often biphasic or triphasic in morphology, are superimposed on a slow and disorganized background rhythm.

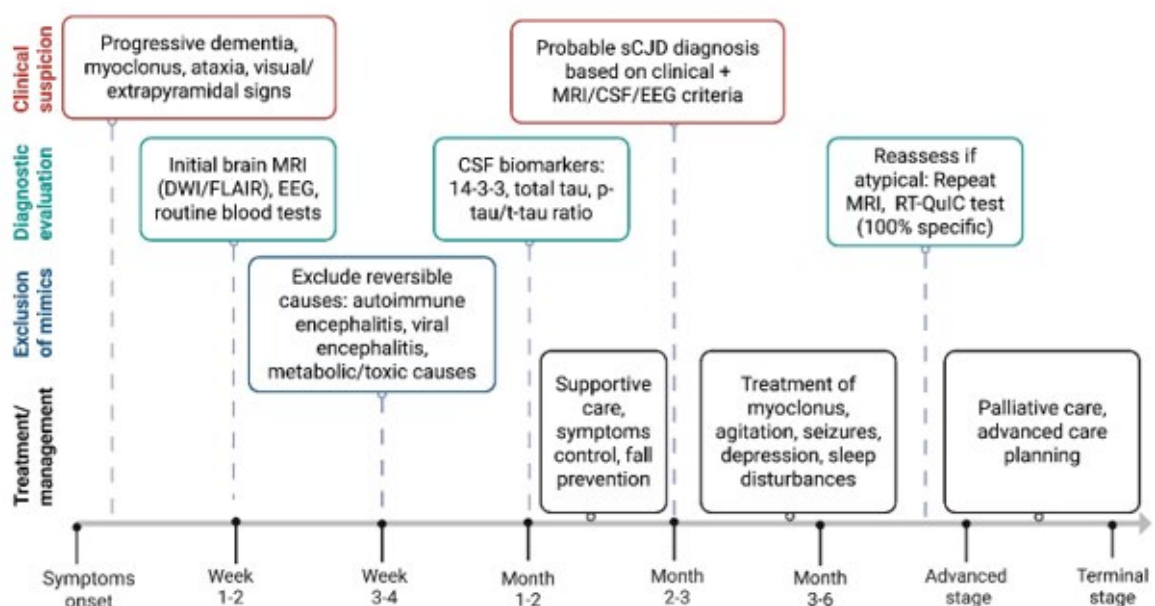


Figure 3. Schematic timeline of clinical progression, diagnostic evaluation, exclusion of mimics, and management in patients with suspected sporadic CJD.

Table 1. Novel therapeutic approaches.

Strategy	Mechanism / Target	Evidence	Current Status / Challenges
Monoclonal Antibodies (PRN100) [72-75]	Bind PrP ^C to block conversion or PrP ^{Sc} to promote clearance	Phase I trial in 6 UK patients: safe, reduced PrP ^{Sc} at autopsy	No clinical benefit yet; risk of neurotoxicity; refinement needed
Antisense Oligonucleotides (ASOs) [76-79]	Reduce PrP ^C expression by degrading PRNP mRNA	In prion-infected mice: 55–100% survival extension; less effective post-onset	Human Phase I trials planned (familial CJD first); delivery and timing challenges
RNA Interference (RNAi) [80]	Viral vector–mediated PRNP silencing	Prolonged survival in animal models	Not yet in human trials; gene therapy risks
PrP^C Stabilizers & Small Molecules [81-84]	Stabilize normal PrP; enhance clearance via proteasome/lysosome (e.g. PROTACs, LYTACs, AUTACs)	Preclinical models; Hsp70 upregulation protective	Still experimental; no approved agents
Active Immunization (Vaccines) [85-89]	Induce anti-PrP immune response	Animal models show immune responses	Risk of autoimmunity; currently theoretical; potential use in high-risk groups or pre-symptomatic genetic carriers
Stem Cell Therapy [90-93]	Neural/mesenchymal stem cells for repair or anti-inflammatory effects	Mice: neural stem cells prolonged survival; mesenchymal cells reduced inflammation but no survival benefit	Not clinically feasible yet; organoids and iPSCs are now used as research models

Table 2. Differential diagnosis of rapidly progressive dementia. Selected conditions and key distinguishing features.

Condition	Distinguishing Features (vs. sCJD)
Rapidly progressive Alzheimer's disease [103,104]	Unusual, rapidly progressive form of AD that can resemble CJD. Progression occurs over many months to a few years (vs. weeks in sCJD). Prominent memory impairment and disorientation; myoclonus uncommon early. MRI: diffuse atrophy (especially hippocampal), no cortical DWI hyperintensities. EEG: diffuse slowing, no periodic complexes. CSF: amyloid-β42 low, p-tau high; RT-QuIC negative; 14-3-3 normal or mildly ↑; t-tau/p-tau ratio high (contrast: low ratio in CJD).
Dementia with Lewy bodies (DLB) [105]	Typically, a gradual dementia over years; RPD is rare but possible. Key features: visual hallucinations and REM sleep behavior disorder common in DLB, less so in CJD. Myoclonus may occur but later and less prominent than in CJD. MRI: diffuse atrophy; no cortical DWI hyperintensities. DaT SPECT: dopaminergic deficit (absent in CJD). EEG: generalized slowing, occasional sharp waves, no periodic complexes. CSF: mild ↑ tau, RT-QuIC negative. Survival often 5–8 years.
Frontotemporal dementia (FTD) [106]	Onset often <65 years with personality change, executive dysfunction, or language impairment. Typically, insidious over 1–2 years, but some cases (e.g., with motor neuron disease) progress faster. Distinguished by focal cortical deficits (behavioral disinhibition, aphasia) early, rather than global cognitive impairment. MRI: focal frontal/anterior temporal atrophy; no cortical DWI hyperintensity. EEG: often normal or mildly slowed early. CSF: lacks prion markers; neurodegenerative panel or genetic testing may confirm diagnosis. Progression usually 2–5+ years, longer than sCJD.
Autoimmune encephalitis (e.g. anti-NMDA receptor, LGI1, GABA_B, Steroid-responsive encephalopathy associated with autoimmune thyroiditis / Hashimoto's encephalopathy) [18]	Subacute dementia with psychiatric symptoms, seizures, or fluctuating consciousness; can resemble CJD. CSF: inflammatory changes (lymphocytic pleocytosis, oligoclonal bands) vs. bland CSF in CJD. MRI: mesial temporal T2-FLAIR hyperintensity or cortical enhancement (not CJD diffusion pattern), sometimes normal or nonspecific. MRI. EEG: seizure activity or extreme delta brush (anti-NMDAR) rather than periodic complexes. Serum/CSF: neural antibodies (e.g., NMDAR, AMPAR, LGI1, CASPR2, GAD65). Improves with immunotherapy (steroids, IVIG, plasmapheresis, rituximab), unlike CJD. Elevated anti-thyroid antibodies; potential clinical improvement with corticosteroids.
Viral encephalitis (e.g. HSV, HHV-6) [107]	Acute or subacute onset (days–weeks) with fever (absent in CJD), confusion, and seizures. CSF: marked pleocytosis and high protein (vs. bland CSF in CJD). MRI: focal temporal lobe edema with contrast enhancement. EEG: periodic lateralized epileptiform discharges (different from generalized PSWC in CJD). CSF PCR: confirms viral etiology. Crucially, antiviral therapy (acyclovir) dramatically improves outcome, so rapid exclusion is essential.
Vascular etiologies (multi-infarct dementia, vasculitis, CNS lymphoma) [17,100,106-108]	Stepwise or abrupt decline suggests strokes; MRI: acute or multiple infarcts in strategic locations (vs. diffuse DWI changes in CJD). CNS vasculitis or intravascular lymphoma can mimic CJD but usually present with focal deficits and atypical MRI lesions (white matter or enhancing lesions). Primary CNS lymphoma shows contrast-enhancing periventricular lesions; confirmed by CSF cytology or biopsy. Intravascular lymphoma may elevate CSF 14-3-3 but RT-QuIC remains negative. Suspicious cases warrant malignancy workup (MRI, CSF cytology, PET/CT) since lymphoma is treatable with chemotherapy.
Toxic-Metabolic encephalopathies (Wernicke's) [102,109]	Metabolic derangements can cause rapid dementia or encephalopathy that reverses with treatment. Wernicke's encephalopathy: confusion, ataxia, eye movement abnormalities; MRI shows mammillary body/periaqueductal changes; improves with IV thiamine. Hyponatremia/rapid sodium shifts: extrapontine myelinolysis with basal ganglia lesions resembling CJD but reversible. Toxins (e.g., lead) or drug toxicity: subacute cognitive decline with systemic clues (lead: GI symptoms, neuropathy; certain drugs: ataxia/confusion resolving after withdrawal). Thorough labs (metabolic panel, vitamins, toxin screens) identify these reversible causes.

approach. Orru et al. reported that nasal brushing RT-QuIC can detect prion seeding activity with high diagnostic performance and may be particularly attractive because the olfactory epithelium may contain higher concentrations of pathological prion seeding activity than CSF. However, nasal brushing RT-QuIC is not yet widely available in routine clinical practice and requires standardized sampling, laboratory expertise, and further validation across broader clinical cohorts. Therefore, CSF RT-QuIC remains the principal clinically established prion seed amplification assay, whereas olfactory mucosa RT-QuIC represents a promising complementary or future diagnostic tool.

14-3-3 Protein: 14-3-3 is a neuronal injury marker released into CSF during acute neuronal damage and detected by Western blot or ELISA. A positive test supports sCJD but lacks specificity because stroke, encephalitis, and severe metabolic encephalopathy can also increase CSF 14-3-3 [23]. Sensitivity is ~85-94% and specificity ~66-84%, with higher specificity reported for ELISA than older blot methods [24,25]. Clinically, a negative result reduces the likelihood of CJD but does not exclude it, while a strongly positive result in a patient with rapidly progressive dementia and typical MRI findings is highly suggestive [23]. Due to false positives, 14-3-3 cannot confirm CJD alone but remains a supportive test in diagnostic criteria [26].

Total Tau and Phospho-tau: Total tau (t-tau) is typically markedly elevated in CJD, often exceeding 1200-1300 pg/mL, reflecting rapid neuronal destruction [24,27]. Proposed cutoffs (~1100-1600 pg/mL) help distinguish CJD from Alzheimer's disease (AD) [27]. In contrast, phosphorylated tau (p-tau) is usually normal or only mildly increased in CJD, whereas it is disproportionately elevated in AD; thus, a low p-tau/t-tau ratio favors CJD. A t-tau/p-tau ratio <0.05 (or <0.075 in some reports) has shown high sensitivity (~96%) and very high specificity (98-100%) for differentiating CJD from AD [28]. Very high tau levels may also vary by molecular subtype (highest in MM1, MV1, and VV2) and correlate with shorter survival [29,30].

Other Investigational CSF Markers: Several additional proteins are increased in sCJD. Alpha-synuclein may be markedly elevated (often >3300 pg/mL) with ~90% sensitivity [31]. Neurofilament light chain (NfL) is also increased (cutoff ~7000 pg/mL; ~85% sensitivity) but is less specific because it rises in many neurodegenerative disorders [32]. Markers of gliosis and inflammation - including YKL-40 (CHI3L1), chitinase-1, and GFAP - are consistently higher in CJD CSF [33-35]. Other candidates (e.g., neurogranin, ubiquitin, calmodulin, and enzymes such as malate dehydrogenase) have been reported to be elevated and may eventually support subtype stratification or disease monitoring, but they are not yet used routinely [34,36-39].

Prognostic Factors, Clinical Progression, and Outcomes:

Prognosis in sporadic Creutzfeldt-Jakob disease (sCJD) is uniformly poor, but disease tempo varies substantially. Most patients progress from symptom onset to death within months, with median survival typically ~4-6 months (2) and <15% surviving beyond one year [40]. Courses range from fulminant illness lasting weeks to rare "long survivors" reported living 2-10 years, producing a right-skewed survival distribution [41].

Age: sCJD most often affects older adults, with median onset around 65-70 years, though cases <50 years occur [42]. In a UK cohort, patients <50 had modestly longer median survival (5.6 vs 4.1 months) [43]. Younger patients more frequently presented with psychiatric symptoms and had later emergence of some neurological deficits [44,45], whereas older age was associated with faster clinical decline [44].

PRNP Codon 129: The PRNP codon 129 polymorphism (methionine [M] or valine [V]) strongly influences susceptibility and prognosis. Although ~50% of the general population is M/V heterozygous, ~70-80% of sCJD cases are homozygous - especially M/M - consistent with increased risk in homozygotes [46]. Codon 129 also predicts disease duration: M/V generally has the longest survival, V/V intermediate, and M/M the shortest, with M/M showing the fastest decline [47,48]. This has been interpreted as a protective effect of heterozygosity and potentially more efficient prion replication in homozygous states [49]. Codon 129 is the strongest established prognostic factor in sCJD and is commonly included in survival prediction models [50]. Together with the abnormal prion protein type (type 1 vs 2), it also defines the major molecular subtypes of sCJD, which show distinct clinical trajectories [51,52].

Molecular Subtype (PrP^{Sc} type and genotype): sCJD is classified into at least six molecular subtypes based on codon 129 genotype (MM, MV, VV) and pathological prion protein type (type 1 or 2) [51]. The major subtypes (MM1, MM2, MV1, MV2, VV1, VV2) are associated with different clinical phenotypes and progression rates; for instance, early visual symptoms (Heidenhain variant) are often linked to MM1 or MV1, while early extrapyramidal features with thalamic MRI changes (Stern-Garcin variant) are more typical of VV2 [52]. Subtype can also affect diagnostic performance (e.g., occasional RT-QuIC negativity in some MM1 cases) and biomarker profiles, with the highest CSF tau levels usually seen in the most rapidly progressive forms (MM1, MV1, VV2) [53-55]. Although prion typing and genotyping are often confirmed postmortem, clinical recognition of subtype patterns supports prognostication; overall, MV2 and VV1 tend to progress more slowly, whereas MM1 is typically the fastest [56-61].

Emerging Treatments and Management Strategies:

At present, no approved treatment can cure or slow sporadic CJD, and management remains largely supportive [62]. Nevertheless, significant efforts have been made to find effective therapies, and several experimental approaches have been explored. This section reviews both palliative care strategies and emerging therapies (including clinical trial results and novel hypotheses). Given the rapid and devastating progression of sporadic Creutzfeldt-Jakob Disease (sCJD), comprehensive supportive care is essential. A multidisciplinary approach is recommended to optimize patient comfort, safety, and dignity while addressing the complex symptom burden. A calm environment - characterized by soft lighting and minimal sensory disturbances - is advised to mitigate distress. As cognitive and motor impairments worsen, close supervision is necessary to prevent falls. In advanced stages, proactive measures should be implemented to prevent pressure ulcers, aspiration, and musculoskeletal contractures, including appropriate feeding

support and positioning strategies. Myoclonus is a frequent manifestation and may be managed with benzodiazepines or valproate, though caution is warranted as sedatives can exacerbate confusion and gait instability. Psychiatric symptoms such as hallucinations or agitation may require antipsychotic therapy; atypical agents like low-dose quetiapine are preferred due to a lower risk of worsening extrapyramidal symptoms compared to typical neuroleptics such as haloperidol. Depression and anxiety may be treated with selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). For sleep disturbances, melatonin or sedating antidepressants (e.g., trazodone) are considered safer alternatives to conventional hypnotics. Although seizures are uncommon, they should be treated with anticonvulsants when present [62]. Over the past two decades, multiple drugs have been tested in sCJD through clinical trials or compassionate use including: flupirtine [63], quinacrine [64], pentosan polysulfate [65], doxycycline [66], immunoglobulins, memantine, creatine [67-71]. However, none of these have demonstrated a definitive benefit on disease progression or survival to date [63-67]. Given the failure of conventional drugs, researchers are pursuing novel strategies targeting the prion itself or modulating the host's handling of misfolded proteins [72-93] (Table 1).

Current consensus emphasizes that early intervention is critical for diagnostic accuracy, infection control, and enrolment in future therapeutic trials, but it does not improve survival because extensive irreversible brain damage has typically occurred by symptom onset, and no disease-modifying therapies exist [94-96]. Improving early diagnosis through sensitive biomarkers and sharing data via international surveillance networks is essential to enable timely trial enrollment [97,98]. Combination strategies may be required, such as pairing a PrP-lowering drug with an antibody to clear existing prions. The field is moving toward innovative trial designs and global collaboration given the rarity of CJD [97,99]. Although no cure currently exists, ongoing research and deeper understanding of prion biology hold promise for future breakthroughs.

Differential Diagnosis of Rapidly Progressive Dementia:

One of the most important steps in evaluating suspected sCJD is to exclude other causes of rapidly progressive dementia (RPD). While most common dementias such as Alzheimer's, Lewy body, and frontotemporal dementia typically have a gradual course [100], several neurological disorders can mimic sCJD with subacute cognitive decline. Key differential diagnoses include autoimmune limbic encephalitis (e.g., anti-LGI1, anti-NMDA, paraneoplastic syndromes), which often present with psychiatric symptoms, seizures, and medial temporal lobe hyperintensities on MRI [101]; steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT/Hashimoto's encephalopathy), particularly in patients with thyroid disease and elevated antithyroid antibodies, as it responds dramatically to corticosteroids [102]; and vascular cognitive impairment due to multi-infarct dementia or strategic strokes, especially in patients with vascular risk factors or imaging evidence of infarcts [100]. Table 2 summarizes the major differential diagnoses for RPD with distinguishing clinical and imaging features.

Limitations.

This review has several limitations. First, although a structured search strategy was used, the article was designed as a narrative review and did not include formal PRISMA-based study selection, risk-of-bias assessment, or quantitative meta-analysis. Second, the available evidence on sCJD is heterogeneous and consists largely of surveillance data, case series, observational studies, diagnostic accuracy studies, and narrative or systematic reviews. Third, neuropathological confirmation was not available in all included studies, and diagnostic criteria have changed over time with the increasing use of DWI MRI and RT-QuIC. Fourth, restriction to English-language publications may have introduced selection bias. These limitations should be considered when interpreting the conclusions of this review.

Conclusion.

Sporadic Creutzfeldt-Jakob Disease (sCJD) remains a major diagnostic challenge due to its rapid progression, fatal outcome, and overlap with other neurological disorders. Advances in MRI and CSF assays, particularly RT-QuIC, have improved ante-mortem diagnosis and reduced reliance on invasive procedures. Clinical variability driven by prion subtypes and host genetics influences presentation and survival, which typically spans only a few months. While no curative therapies exist, research into antiprion antibodies, gene-silencing, and other strategies offers hope. Current care is supportive, emphasizing symptom management and trial enrollment. Continued international surveillance, collaborative research, and high-quality observational data are essential to refine diagnostics and advance therapeutic development.

Conflicts of Interest.

The authors declare no conflicts of interest.

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