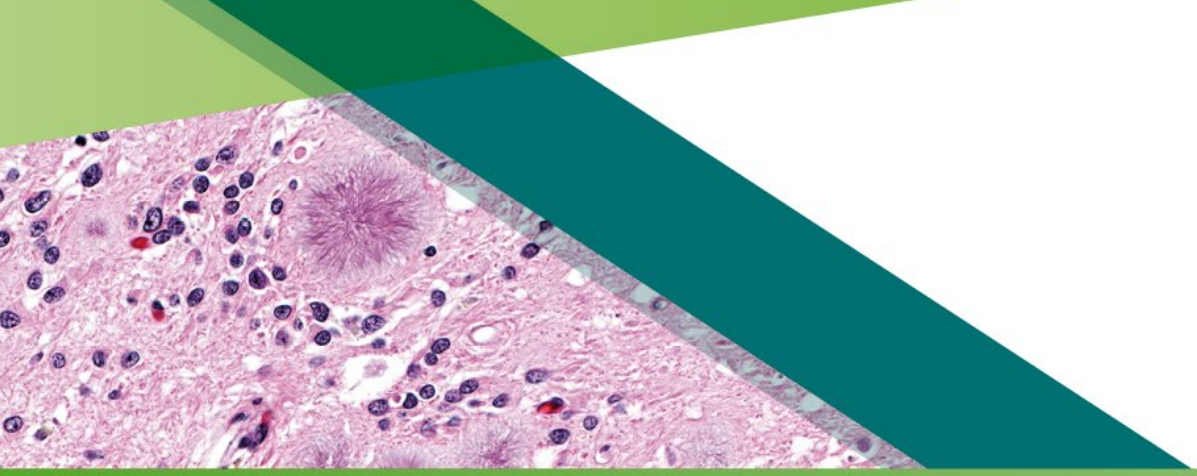

SURVEILLANCE REPORT

Annual Epidemiological Report for 2022

Variant Creutzfeldt-Jakob disease

Key facts

- In 2022, there were no reported cases of variant Creutzfeldt-Jakob disease (vCJD) in the EU/EEA.
- In total, 28 EU/EEA countries reported data on vCJD in 2022.
- Variant Creutzfeldt-Jakob disease remains extremely rare. This is consistent with the current understanding of the underlying epidemiology of vCJD, and the positive impact of risk mitigation measures introduced in the EU from the late 1980s to remove potentially infectious animal material from the food chain, to prevent infections in humans.

Introduction

Variant Creutzfeldt–Jakob disease (vCJD) is a prion disease, a group of rare neurological diseases caused by abnormal misfolded prion proteins (PrPSc). These abnormal prions accumulate in the brain and lead to progressive brain damage, causing psychiatric or sensory symptoms, neurological abnormalities and eventual death. vCJD was first identified in the United Kingdom, and in March 1996, an association was found between vCJD and the consumption of products from animals infected with bovine spongiform encephalopathy (BSE), known as 'mad cow disease' [1]. Hence, the most likely route of transmission is through the consumption of BSE-infected meat and meat products. Secondary transmission of variant Creutzfeldt-Jakob disease (vCJD) has also been reported in rare cases – e.g. following blood transfusions or receipt of plasma-derived products from infected donors. These cases occurred before safety measures were introduced in the 1990s to remove potentially contaminated blood components.

Methods

This report is based on data for 2022 retrieved from The European Surveillance System (TESSy) on 2 February 2024. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases.

For a detailed description of methods used to produce this report, refer to the 'Methods' chapter [2].

An overview of the national surveillance systems is available online [3].

A subset of the data used for this report is available through ECDC's online 'Surveillance atlas of infectious diseases' [4].

The ECDC-operated TESSy database includes individual case data from all vCJD cases diagnosed in the EU. Prospective reporting of 'probable' or 'confirmed' new cases is done in accordance with the 2012 EU case definition.

The clinical presentation and associated diagnostic criteria for vCJD are relatively unusual. Suspected cases are typically reported to national surveillance centres. The centres offer diagnostic support and post-mortem analysis when needed. Ultimately, successful vCJD surveillance requires the identification of patients as 'possible' CJD cases, supported by accurate differential diagnosis between vCJD and other more common forms of CJD (sporadic, iatrogenic and familial).

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A further diagnostic constraint is the need to obtain appropriate tissue samples post-mortem to determine neuropathological characteristics associated with vCJD. In many cases, such tissue is not available and in these situations, cases can only be classified as 'possible' or 'probable', based on the clinical and diagnostic criteria available.

Cases reported here are restricted to 'confirmed' and 'probable'.

Epidemiology

For 2022, 28 EU/EEA countries reported data on vCJD and none reported human vCJD cases (Table 1).

Table 1. Variant Creutzfeldt-Jakob disease cases by country and year, EU/EEA, 2018–2022

Country	2018	2019	2020	2021	2022
Austria	0	0	0	0	0
Belgium	0	0	0	0	0
Bulgaria	0	NDR	NDR	0	0
Croatia	0	0	0	0	0
Cyprus	0	0	0	0	0
Czechia	0	0	0	0	0
Denmark	0	0	0	0	0
Estonia	0	0	0	0	0
Finland	NDR	NDR	NDR	NDR	NDR
France	1	0	0	1	0
Germany	NDR	NDR	NDR	NDR	NDR
Greece	0	0	0	0	0
Hungary	0	0	0	0	0
Iceland	0	0	0	0	0
Ireland	0	0	0	0	0
Italy	0	0	0	0	0
Latvia	0	0	0	0	0
Liechtenstein	NDR	NDR	NDR	0	0
Lithuania	0	NDR	0	0	0
Luxembourg	0	0	0	0	0
Malta	0	NDR	NDR	0	0
Netherlands	0	0	0	0	0
Norway	0	0	0	0	0
Poland	0	0	0	0	0
Portugal	0	0	0	0	0
Romania	0	0	0	0	0
Slovakia	0	0	0	0	0
Slovenia	0	0	0	0	0
Spain	0	0	0	0	0
Sweden	0	0	0	0	0
EU/EEA (30 countries)	**1**	**0**	**0**	**1**	**0**
United Kingdom	0	0	NA	NA	NA
EU/EEA (31 countries)	**1**	**0**	**0**	**1**	**0**

Source: Country reports.
NDR: No data reported.
NA: Not applicable.
From 2020 onwards, no data were reported by the United Kingdom, due to its withdrawal from the EU on 31 January 2020.

Outbreaks and other threats

In 2022, no national or multicounty vCJD outbreaks were reported in EpiPulse.

Secondary transmission of vCJD can occur through blood transfusion or receipt of plasma-derived products. To date, five patients have been suspected of having acquired clinical vCJD or a vCJD infection after receiving a blood or plasma-derived product from a donor who later developed clinical vCJD [6]. The possibility of asymptomatic cases among the patients who received blood transfusions raises the concern that prions might be present in many other carriers who may never develop vCJD, but can transmit the disease. This requires specific preventive procedures to minimise the risk of secondary transmission of vCJD [7].

Discussion

The vCJD epidemic peaked in the EU between 1999 and 2004. Since then, vCJD has become a very rare neurodegenerative disease in the EU/EEA. This is due to the successful implementation of prevention and control measures to remove bovine spongiform encephalopathy (BSE) prions from human and animal food chains in the late 1980s and 1990s.

There is still some uncertainty regarding the epidemiology and public health risk from vCJD. The absence of a definitive diagnostic test means that accurate prevalence estimates for vCJD infection in EU populations remains elusive. Some studies on prevalence of abnormal prion protein in the human appendix, conducted in the UK, suggest that the underlying prevalence of sub-clinical vCJD infection in the general population is in the order of 0.05%, (493 cases per one million population) [9]. However, there is a great deal of uncertainty surrounding this estimate. The contrast between the estimated prevalence of vCJD-related PrPSc (pathological 'scrapie' isoform of the prion protein (PrP)) and the reported number of clinical vCJD cases seen to date strongly suggests that those in whom PrPSc is detected through an antemortem lymphoid tissue survey may never develop any symptoms of prion disease. Furthermore, in 2016, the first confirmed vCJD case in a clinical patient expressing heterozygosity at codon 129 of the human prion protein gene was identified [10]. All previous vCJD cases were identified in homozygous individuals. Therefore there is a theoretical possibility that MV heterozygotes (i.e. those carrying the Methionine (M)/Valine (V) single nucleotide polymorphism (SNP) at position 129 of the human prion protein gene), which make up approximately 50% of the EU population, may also be potentially susceptible to infection but that the MV genotype may confer longer incubation periods [11]. Hence, the possibility remains that there is a cohort of infected individuals in the EU population who may develop the disease or cause secondary transmission through blood and/or organ donations. This potential public health risk continues to have implications for the management of blood and blood products, transfusion, tissue transplantation, cellular therapies and the handling of surgical instruments [12-14]. However, the consistently low prevalence of clinical cases of vCJD over a number of years offers reassurance that a large-scale epidemic of vCJD in the EU is increasingly unlikely.

As vCJD is associated with the transmission of BSE from infected animals, ongoing assessment of the epidemiology of prion diseases in animals and potential zoonotic transmission is important for public health. The EU Member States are therefore continuing to implement an annual targeted surveillance programme, coordinated by the European Food Safety Authority, to assess the prevalence of Transmissible Spongiform Encephalopathies (TSE) infection in animal populations [5]. In 2022, a total of 977 008 cattle were tested by EU Member States (EU27) and the UK (in respect of Northern Ireland (XI)). In the EU27 and XI, one atypical BSE case was confirmed in 2022 by France. This was a case of H-BSE in a 154-month-old beef bovine animal. No other BSE cases were reported worldwide in 2022. Overall, the low prevalence of positive cases identified by EU surveillance strongly indicates that there are very few BSE-infected animals in EU cattle populations and therefore the public health risk of vCJD infection from consumption of beef in the EU appears very low.

Further details on TSE surveillance in EU animal populations in 2022 is available in 'The European Union summary report on surveillance for the presence of transmissible spongiform encephalopathies (TSE) in 2022' [5].

Public health implications

Twenty-five years has now passed since vCJD was first described in the UK. Due to the potential risk of secondary infection via transfusion, many countries have imposed restrictions on blood donation from people with potential exposure risk through prior residency in, or extended travel to the UK and/or other countries recording vCJD cases [15]. However, reviews of modelling studies [15, 6] have shown that the risks of vCJD transmission (infection) were one in 389 000 000, the risk of a clinical case was one in 1 450 000 000, the risk of collecting a contaminated donation was generally <23 per million donations, that of infection was generally <10 per million transfusions or doses, and that of clinical vCJD was generally <2 per million transfusions or doses. In addition, the two-decade-long absence of new cases of transfusion-associated vCJD suggests that the disease poses a minimal risk to the safety of the blood supply [6].

Public health measures are developed on the assumption that all population groups are susceptible to vCJD infection and clinical disease, and the continued absence of clinical cases of vCJD in the EU strongly indicates that EU-wide protection measures against prion disease infection continue to be effective. However, some uncertainties remain. The extended incubation period mean there might be decades between infection and clinical manifestation of vCJD. A definitive diagnosis of vCJD can be only be made postmortem, however technologies in screening tests such as the PMCA (protein misfolding cyclic amplification) can be used to trace PrP^{Sc} in the urine, blood and cerebrospinal fluid (CSF) of vCJD patients in the antemortem stage as well. The absence of a rapid diagnostic test means that the infection status of the EU population is unclear.

There may also be an elevated vCJD risk from certain exposure routes, as indicated by the recent cases associated with occupational exposure in laboratory environments. This suggests that certain occupational exposures may present a viable route for vCJD transmission, and laboratory practices in environments where known TSE-infected material is present should take account of this potential risk. In addition, the nature of CJD infection implies that the clinical presentation of disease in infected patients exposed through non-dietary routes, or an infectious agent that is not BSE-derived, may differ from that of vCJD. It is therefore important that there is continued human and animal surveillance at the national and EU-level to monitor all forms of CJD and other human prion diseases in order to identify possible sources of public health risk. Monitoring will provide assurances that public health measures to minimise risk of vCJD infection in EU populations are effective; that risk profiles from vCJD and other prion diseases remain unaltered, and that changes which may affect public health can be detected [17, 18].

References

1. Will RG, Ironside JW, Zeidler M, Cousens SN, Estibeiro K, Alperovitch A, et al. A new variant of Creutzfeldt-Jakob disease in the UK. Lancet. 1996 Apr 6;347(9006):921-5. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8598754
2. European Centre for Disease Prevention and Control (ECDC). Introduction to the Annual Epidemiological Report for 2016. Stockholm: ECDC; 2017. Available at: https://ecdc.europa.eu/en/annual-epidemiological-reports-2016/methods
3. European Centre for Disease Prevention and Control (ECDC). Surveillance Systems Overview [downloadable spreadsheet]. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/sites/portal/files/documents/Table-surveillance_systems_overview_for_2016.xlsx
4. European Centre for Disease Prevention and Control (ECDC). Surveillance Atlas of Infectious Diseases. Stockholm: ECDC; 2017. Available at: http://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=27
5. European Food Safety Authority (EFSA). The European Union summary report on surveillance for the presence of transmissible spongiform encephalopathies (TSE) in 2022, EFSA Journal. 2023;21:e8384, published by Wiley-VCH GmbH on behalf of European Food Safety Authority. Available at: https://doi.org/10.2903/j.efsa.2023.838
6. Pozzo di Borgo A, Rochette S, Gaussen A, O'Brien SF, Germain M, Renaud C, Lewin A. Transmission of Variant Creutzfeldt-Jakob Disease Through Blood Transfusion and Plasma-Derived Products: A Narrative Review of Observed and Modeled Risks. Transfus Med Rev. 2023 Jul;37(3):150747. doi: 10.1016/j.tmrv.2023.150747. Epub 2023 Jun 16. PMID: 37827587.
7. Giaccone G, Moda F. PMCA Applications for Prion Detection in Peripheral Tissues of Patients with Variant Creutzfeldt-Jakob Disease. Biomolecules. 2020 Mar 5;10(3):405. doi: 10.3390/biom10030405. PMID: 32151109; PMCID: PMC7175161. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7175161/
8. The National CJD Research & Surveillance Unit, Western General Hospital, UK. 31st Annual Report 2022 Creutzfeldt-Jakob Disease Surveillance in the UK. Available at: https://www.cjd.ed.ac.uk/sites/default/files/report31.pdf
9. Gill ON, Spencer Y, Richard-Loendt A, Kelly C, Dabaghian R, Boyes L, et al. Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey. BMJ. 2013 Oct 15;347:f5675. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24129059
10. Mok T, Jaunmuktane Z, Joiner S, Campbell T, Morgan C, Wakerley B, et al. Variant Creutzfeldt-Jakob Disease in a Patient with Heterozygosity at PRNP Codon 129. N Engl J Med. 2017 Jan 19;376(3):292-4. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28099827
11. Garske T, Ghani AC. Uncertainty in the tail of the variant Creutzfeldt-Jakob disease epidemic in the UK. PLoS One. 2010 Dec 23;5(12):e15626. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21203419
12. Brown P, Brandel JP, Sato T, Nakamura Y, MacKenzie J, Will RG, et al. Iatrogenic Creutzfeldt-Jakob disease, final assessment. Emerg Infect Dis. 2012 Jun;18(6):901-7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22607808
13. Head MW. Human prion diseases: molecular, cellular and population biology. Neuropathology. 2013 Jun;33(3):221-36. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23331517
14. Roberts PL, Dalton J, Evans D, Harrison P, Li Z, Ternouth K, et al. Removal of TSE agent from plasma products manufactured in the United Kingdom. Vox Sang. 2013 May;104(4):299-308. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23170907
15. McManus H, Seed CR, Hoad VC, Kiely P, Kaldor JM, Styles CE, Yang H, Law M, Gosbell IB. Risk of variant Creutzfeldt-Jakob disease transmission by blood transfusion in Australia. Vox Sang. 2022 Aug;117(8):1016-1026. doi: 10.1111/vox.13290. Epub 2022 May 24. PMID: 35609012; PMCID: PMC9544957. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9544957/
16. Giaccone G, Moda F. PMCA Applications for Prion Detection in Peripheral Tissues of Patients with Variant Creutzfeldt-Jakob Disease. Biomolecules. 2020 Mar 5;10(3):405. doi: 10.3390/biom10030405. PMID: 32151109; PMCID: PMC7175161. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7175161/
17. Budka H, Will RG. The end of the BSE saga: do we still need surveillance for human prion diseases? Swiss Med Wkly. 2015;145:w14212. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26715203
18. Watson N, Brandel JP, Green A, Hermann P, Ladogana A, Lindsay T, et al. The importance of ongoing international surveillance for Creutzfeldt-Jakob disease. Nat Rev Neurol. 2021 Jun;17(6):362-79. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33972773