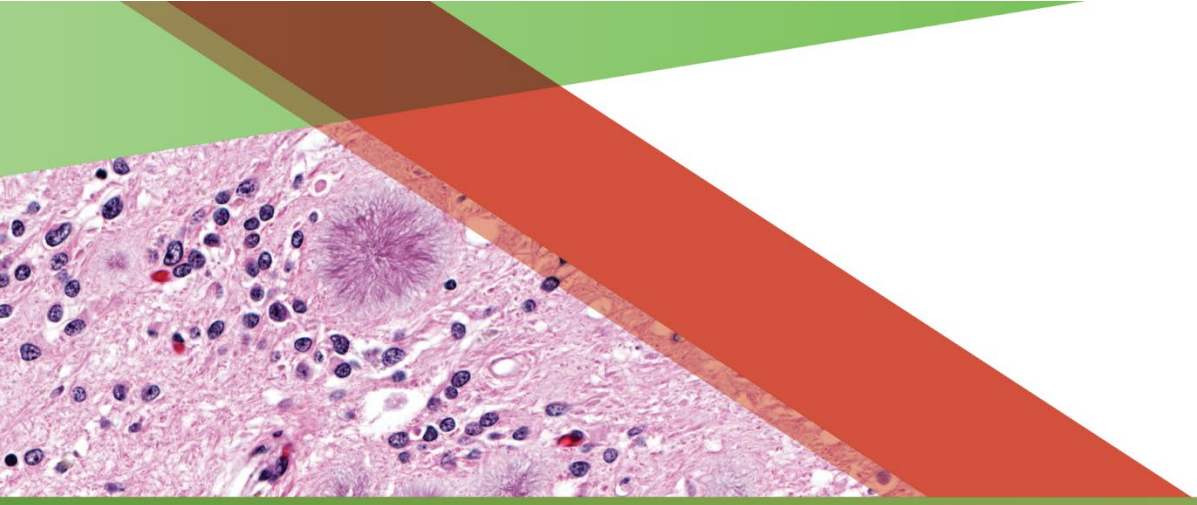

SURVEILLANCE REPORT

Variant Creutzfeldt-Jakob disease

Annual Epidemiological Report for 2021

Key facts

- A single case of variant Creutzfeldt-Jakob disease (vCJD) was reported in the EU/EEA in 2021.
- VCJD disease remains extremely rare. This is consistent with the current understanding of the underlying epidemiology of vCJD, and with 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 (UK), and in March 1996 an association was identified between vCJD and the consumption of products from animals infected with bovine spongiform encephalopathy (BSE), also known as 'Mad Cow Disease' [1].

Methods

This report is based on data for 2021 retrieved from The European Surveillance System (TESSy) on 9 October 2022. 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.

The EU case definition for vCJD reporting to TESSy is restricted to 'confirmed' and 'probable' cases. Only these cases are included in ECDC's Surveillance Atlas and in this report.

Epidemiology

A single case of vCJD was reported in the European Union/European Economic Area (EU/EEA) in 2021. The case was classified as a probable vCJD case and was reported by France. The infected person first displayed symptoms during the year and died in November 2021. The case was reported to have performed laboratory work with biological tissues infected with prions before retirement, and hence potential occupational exposure could be suspected [5].

One previous case was reported by France, in 2018 (Table 1). The overall mortality rate remains below 0.01 cases per one million population in this long post-epidemic tail.

Table 1. Number of variant Creutzfeldt-Jakob disease cases by country and year, EU/EEA, 2017–2021

Country	2017	2018	2019	2020	2021
	Number		Number		Number
Austria	0	0	0	0	0
Belgium	0	0	0	0	0
Bulgaria	0	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	0	1	0	0	1
Germany	NDR	NDR	NDR	NDR	NDR
Greece	0	0	0	0	0
Hungary	0	0	0	0	0
Iceland	0	0	0	0	NDR
Ireland	0	0	0	0	0
Italy	0	0	0	0	0
Latvia	0	0	0	0	0
Liechtenstein	NDR	NDR	NDR	NDR	0
Lithuania	0	0	NDR	0	0
Luxembourg	0	0	0	0	0
Malta	0	0	NDR	NDR	0
Netherlands	0	0	0	0	NDR
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	NDR
Slovenia	0	0	0	0	0
Spain	0	0	0	0	0
Sweden	0	0	0	0	0
United Kingdom	0	0	0	NDR	NDR
EU/EEA	0	1	0	0	1

Source: Country reports. NDR: no data reported.

Outbreaks and other threats

In February 2021, the UK lifted its ban on the use of UK-sourced plasma to produce immunoglobulin products [6]. The UK assessed the vCJD risk for immunoglobulin products manufactured from UK plasma as very low and acceptable in the context of overall vCJD risk in the general population, taking into consideration a risk-benefit analysis [7].

Following the decision by the UK, the European Commission requested that ECDC conduct a risk assessment on 'The risk of variant Creutzfeldt-Jakob disease transmission via blood and plasma-derived medicinal products (PDMPs) manufactured from donations obtained in the United Kingdom'. The assessment concluded that the vCJD infection risk from the donations and final products is decreased by the safety measures implemented to reduce the risk of donation by exposed donors and during whole blood processing or plasma fractionation. However, the absence of a reliable diagnostic blood test makes it difficult to assess the residual risk for transmission of vCJD infection through blood components and PDMPs obtained from UK-sourced blood and plasma donations with any degree of confidence. Hence, in order to determine whether the use of immunoglobulins and other PDMPs produced from UK plasma would pose an increased threat, EU/EEA countries may consider 'assessing their endogenous risks, evaluating product-specific data packages (including the prion-reduction capacities of applied fractionation procedures), and balancing the assessed threat with the supply need for PDMPs and source plasma in their country. Until such data are available, EU/EEA countries may consider, as a precautionary measure, preventing the use of immunoglobulins and other PDMPs derived from UK plasma, as well as the fractionation of UK plasma in EU/EEA facilities' [8].

Further investigations of the possible cause of the vCJD case reported by France in 2021 indicated that a plausible source of infection was an accidental occupational exposure in a laboratory environment. This is the third vCJD case in recent history that has an association with laboratory exposure to transmissible spongiform encephalopathy (TSE) agents following two vCJD cases reported in France in 2018 and Italy in 2016 who also had occupational contact with BSE-infected brain tissue.

Discussion

The vCJD epidemic peaked in the EU from 1999–2004, but the number of cases has subsequently decreased. 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 the food chains aimed at the cattle trade (since 1989) and animal feed production (since 1994).

More generally, some uncertainty remains on the epidemiology and public health risk from vCJD. Studies on prevalence of abnormal prion protein in human appendixes conducted in the UK suggest that the underlying prevalence of people that may be in the vCJD carrier state is in the order of 0.05%, (493 cases per one million population) [9]. However, much uncertainty remains around 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 have been identified in homozygous individuals. This suggests 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 potentially be susceptible to infection, but that the MV genotype may confer longer incubation periods [11].

In summary, the consistently low prevalence of clinical cases of vCJD over several years gives reassurance that a large-scale epidemic of vCJD in the EU is increasingly unlikely. There remains the potential that a cohort of infected individuals remains in the EU population who may develop the disease or cause secondary transmission through blood and/or organ donations. This has potential implications in areas such as the management of blood and blood products, transfusion, tissue transplantation, cellular therapies, and the handling of surgical instruments [12-14].

The association of three recent vCJD cases from Italy and France with potential occupational exposure to infected TSE material in laboratory settings highlights that laboratory exposure from transmissible prion agents remains a viable route of transmission [5]. As a result of the case identified in France in 2021, five public research institutions in France imposed a temporary moratorium on the study of prions to assess possible links to potential occupational exposure to prion disease in laboratories and review current laboratory practise to ensure any risk of exposure was minimised [15].

As vCJD is associated with the transmission of BSE from infected animals, the assessment of ongoing epidemiology of prion diseases in animals and potential zoonotic transmission remains important for public health. Hence, EU Member States continue to implement an annual targeted surveillance programme to assess the prevalence of TSE infection in animal populations, coordinated by the European Food Safety Authority (EFSA). In 2021, a total of 1 021 252 cattle were tested by 27 EU Member States and the UK (in respect of Northern Ireland), and a total of six atypical cases of BSE were confirmed: by France (one H-BSE and two L-BSE), Germany (one L-BSE) and Spain

(one H-BSE and one L-BSE). All six cases were born between 2006 and 2009, and none of these animals were destined for the human food chain and so presented no direct risk to public health. Overall, the low prevalence of positive cases identified by EU surveillance strongly indicates that very few BSE-infected animals reside in EU cattle populations. Hence the public health risk of vCJD infection from consumption of cattle in the EU appears low. All six cases are also classified as 'atypical BSE'. The origin of such cases is unclear, but the pathology differs from the 'classical BSE' associated with consumption of contaminated feed, which is believed to be the source of the primary BSE epidemic and subsequent causal association with vCJD cases.

Four additional cases of BSE were reported in the rest of the world in 2021: two by Brazil, one by Canada and one by the UK. The case from the UK was a classic BSE case, detected in a homebred dairy cow born in February 2015.

Following the identification of the first case of chronic wasting disease (CWD) – a TSE that affects cervids (deer, elk and moose) in wild European cervid populations in 2016 [16] – six Member States undertook EU-mandated surveillance in cervid populations between 2018 and 2020 as part of a three-year targeted surveillance program [17]. From 2021, EU Member States and non-EU reporting countries have carried out monitoring for CWD in cervids only on a voluntary basis. In 2021, this resulted in the testing of 5 854 cervids for chronic wasting disease by eight EU Member States; all results were negative. In addition, Norway tested 21 670 cervids with two moose and one red deer positive. Further details on TSE surveillance in EU animal populations in 2021 is available in 'The European Union summary report on surveillance for the presence of transmissible spongiform encephalopathies (TSE) in 2021' [18].

Public health implications

Public health measures are developed on the basis that all population groups are susceptible to vCJD infection and clinical disease, and the continued absence of clinical cases of vCJD in the EU gives confidence that EU-wide protection measures against prion disease infection continue to be effective. However, some uncertainties remain. The extended incubation periods mean there might be decades between infection to clinical manifestation of vCJD. 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 practises 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. Hence prion transmission and circulation within human populations remains a potential risk.

The evolving epidemiology of TSEs in animal populations and potential zoonotic risk from animal TSEs also create some uncertainty for public health. Although TESSy supports data collection of vCJD cases, continued surveillance at the national and EU level to monitor all forms of CJD and other human prion diseases is important 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, risk profiles from vCJD and other prion diseases remain unaltered and changes that may impact public health can be detected [19,20].

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