Available online at www.sciencedirect.com
ScienceDirect
Biologicals 35 (2007) 79–97
IABS BIOLOGICALS
www.elsevier.com/locate/biologicals

Review

Impact of vCJD on blood supply

Rainer Seitz [a,*], Friedger von Auer [b], Johannes Blümel [a], Reinhard Burger [c], Anne Buschmann [d], Klaus Dietz [e], Margarethe Heiden [a], Walter E. Hitzler [f], Horst Klamm [b], Thomas Kreil [g], Hans Kretzschmar [h], Micha Nübling [a], Ruth Offergeld [c], Georg Pauli [c], Volkmar Schottstedt [i], Peter Volkers [a], Inga Zerr [j]

[a] *Paul-Ehrlich-Institut, Paul-Ehrlich-Strasse 51–59, D-63225 Langen, Germany*
[b] *Federal Ministry of Health, Bonn, Germany*
[c] *Robert Koch-Institut, Berlin, Germany*
[d] *Friedrich-Loeffler-Institut, Insel Riems, Germany*
[e] *Department of Medical Biometry, Eberhard-Karls-University, Tübingen, Germany*
[f] *Transfusion Centre, Johannes Gutenberg-University Hospital, Mainz, Germany*
[g] *Baxter AG, Vienna, Austria*
[h] *Centre for Neuropathology and Prion Research, Ludwig-Maximilians-University, Munich, Germany*
[i] *German Red Cross Blood Donation Service West, Hagen, Germany*
[j] *Department of Neurology, Prion Research Group, University Hospital, Göttingen, Germany*

Received 16 November 2006; revised 9 January 2007; accepted 9 January 2007

Abstract

Variant Creutzfeldt–Jakob disease (vCJD) is an at present inevitably lethal neurodegenerative disease which can only be diagnosed definitely post mortem. The majority of the approximately 200 victims to date have resided in the UK where most contaminated beef materials entered the food chain. Three cases in the UK demonstrated that vCJD can be transmitted by blood transfusion. Since BSE and vCJD have spread to several countries outside the UK, it appears advisable that specific risk assessments be carried out in different countries and geographic areas. This review explains the approach adopted by Germany in assessing the risk and considering precautionary measures. A fundamental premise is that the feeding chain of cattle and the food chain have been successfully and permanently cleared from contaminated material. This raises the question of whether transmissions via blood transfusions could have the potential to perpetuate vCJD in mankind. A model calculation based on actual population data showed, however, that this would not be the case. Moreover, an exclusion of transfusion recipients from blood donation would add very little to the safety of blood transfusions, but would have a considerable impact on blood supply. Therefore, an exclusion of transfusion recipients was not recommended in Germany.

Keywords: Bovine spongiform encephalopathy; Variant Creutzfeldt–Jakob disease; Blood supply; Risk assessment

Abbreviations: AFSSAPS, Agence Française de Sécurité Sanitaire des Produits de Santé (French medicinal products authority); BSE, bovine spongiform encephalopathy (degenerative neurological disease in cattle caused by prions); CJD, Creutzfeldt–Jakob disease (TSE disease in humans, transmissible via medicinal products (iatrogenic) or occurring sporadically); FFP, "fresh frozen plasma"(plasma for transfusion); GBR, "geographical BSE risk": classification of countries into one of four risk classes (GBR I–IV) by the Scientific Steering Committee of the European Commission; GSS, Gerstmann-Sträussler-Scheinker syndrome (a human TSE); HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus (agent of AIDS); i.c., intracerebral; IU, infectious unit; i.v., intravenous; M, methionine; PMCA, protein misfolding cyclic amplification (method for amplification of PrP^{Sc} in vitro); PrP, prion protein; PrP^{c}, cellular, physiological form of the prion protein (c = cellular); PrP^{Sc}, pathological form of the prion protein (Sc = Scrapie); RBCC, red blood cell concentrate; SCMPMD, Scientific Committee on Medicinal Products and Medical Devices of the European Commission; SRM, specified risk material (bovine materials in which the BSE agent can be detected in high concentrations (brain, spinal cord etc.)); SSC, Scientific Steering Committee of the European Commission; TSE, transmissible spongiform encephalopathy (disease of the brain, generic term for neurological disorders caused by prions); UK, United Kingdom (Great Britain and Northern Ireland); V, valine; vCJD, variant Creutzfeldt–Jakob disease (human TSE caused by the BSE agent, first described in 1996).

* Corresponding author. Tel.: +49 6103 772600; fax: +49 6103 771250.
E-mail address: seira@pei.de (R. Seitz).

1045-1056/07/$32.00
doi:10.1016/j.biologicals.2007.01.002

1. Introduction

A working group was formed in 2001 by request of the German Federal Ministry of Health that consisted of staffs from the Paul-Ehrlich-Institut, the Robert-Koch-Institut and the Federal Ministry of Health, as well as external experts. The task of this working group has been to assess the risks for the blood supply in Germany with regard to vCJD and to prepare reports outlining a strategy. The spread of bovine spongiform encephalopathy (BSE) among cattle is believed to be the origin of the problem, followed by the transition to humans via the food chain. Since the epidemical course shows geographical differences, every country needs to assess its specific vCJD risk as a condition for developing a reasonable national blood supply strategy. The group published reports[1] in 2001 and in 2006 [1]. This review summarizes the current view of the group of the impact of vCJD on blood supply.

2. The Occurrence of BSE

Feeding of ruminant material to cattle has most probably caused the occurrence of BSE, a disease of cattle that was first diagnosed in the UK in 1986 [2]. Technological changes (pressure and temperature conditions) in the manufacture of meat and bone meal and other products are considered to be the cause for the occurrence of BSE in the UK beginning in 1985, since the inactivation of the BSE pathogen was no longer sufficiently effective [3]. This assumption is confirmed by the course of the epidemic in the UK where a decline in the number of cases was observed during the mid-1990s with a time lag representing the incubation time of 4–5 years for BSE following the ban on the feeding of meat and bone meal and the regulations on the disposal of BSE-infected animal carcasses [4] (Table 1). While in the first few years it was assumed that there was only one strain of BSE in cattle, several authors have described atypical BSE cases in the past few years [5–7]. These cases do not represent a uniform strain and are characterized by an altered molecular weight of the accumulated PrP^{Sc}, a different anatomical distribution pattern of the pathological changes and the PrP^{Sc} deposits, and partly by the occurrence of amyloid plaques. All cases of atypical BSE described so far have been found in animals older than 8 years. The cases described in France show a biochemical similarity with the cases of scrapie in sheep. Therefore, the possibility that these might be scrapie infections in cattle is discussed.

Through animal trade and trade of feeding stuff components produced from animal carcasses and slaughtering by-products (bone meal, fats for milk replacers, grieves etc.), BSE spread from the UK to other European countries and countries outside Europe (e.g. Canada, Japan, Israel). First Ireland (1989), then Switzerland (1990) and France (1991) reported cases of BSE. During the mid-1990s, Portugal (1994), the Netherlands (1997), Belgium (1997), Luxemburg (1997), and Liechtenstein (1998) reported cases. Toward the end of the 1990s, it became clear that almost all countries with extensive exchange of goods within the European single market during the previous decade were affected by BSE. It was, therefore, not surprising that BSE was diagnosed in some cattle of Denmark, Germany, and Spain in the year 2000 and also in Austria, the Czech Republic, Finland, Greece, Italy, Slovakia, and Slovenia in 2001. Since 2002, BSE has also been diagnosed in Polish cattle. Cases of BSE in cattle imported from the UK were reported as early as the early 1990s by several European countries (Portugal 1990, Germany 1992, Denmark 1992, Italy 1994). Three BSE cases have so far occurred in the United States, of which one animal had been imported from Canada. The two indigenous cases were of the atypical BSE type of which the origin is still unknown.

In addition to animal trade and trade with animal products, however, intrinsic national factors influenced the occurrence and spread of BSE. Since by the 1980s most EU member states had changed their animal carcass disposal methods and processed side products from abattoirs without the removal of risk materials under pressure and temperature conditions that were not sufficient for the inactivation of the BSE pathogen, this pathogen was continuously spread, thus increasing the number of BSE cases. Moreover, only passive monitoring systems based on the reporting of clinical symptoms were in place; BSE rapid tests were not yet available.

Organs and tissues of BSE infected cattle in which the pathogen has been detected are called ‘‘specified risk materials’’ (SRM). SRM of naturally infected animals may, especially toward the end of the incubation period and during the development of clinical BSE symptoms, contain the pathogen in very high concentrations. Using biological detection systems for the BSE pathogen, which include a species barrier, e.g. intracerebral infection into mice, 10^5 infectious units/g SRM (brain) were determined, while a 1000-fold increased infectivity titer is assumed for transmissions within a species [8–10]. The Scientific Steering Committee (SSC) of the European Commission set up an SRM list for cattle (e.g. skull including brain and eyes, tonsils, spinal cord) (SSC 1998[2]), which served as a basis for various European policies for the exclusion of SRM in the food and feed chains. Since the spread of the BSE crisis in Europe, the definition of specified risk materials has been revised several times (a comprehensive overview of the European legislation can be found in Table 2 of [1]). According to the latest amendment, the tissues designated as SRM must be subjected to safe removal and must not enter the food chain. The following tissues are designated as SRM: ‘‘The skull excluding the mandible and including the brain and eyes, the vertebral column excluding the vertebrae of the tail, the spinous and transverse processes of the cervical, thoracic and lumbar vertebrae and the wings of the sacrum, but including the dorsal root ganglia, and the spinal cord of

[1] The reports published by this group in German language in the years 2001 and 2006 can be found in the internet: http://www.pei.de.

[2] Scientific Steering Committee (SSC), 1998. Listing of Specified Risk Materials: a scheme for assessing relative risks to man–Opinion of the SSC adopted on 9 December 1997 (Re-edited version adopted by the SSC during its Third Plenary Session of 22–23 January 1998).