not control these combinations. The biological meaning of these aggregations is not known.

The observations from this experiment show that acidic SDS precipitation of plasma preparations enables discrimination between scrapie-infected and mock-infected hamsters and may be an extremely important finding for the developing of an antemortem blood test to diagnose TSE. The question as to why the silent prion is not precipitated by the acidic precipitation if it exists in mcPI remains to be answered.

We gratefully acknowledge Dr. Professor Takashi Onodera, Department of Molecular Immunology, Agricultural and Life Sciences, Tokyo University, for his great support and encouragement, Dr. Yokoyama, Research Center for Prion Diseases, National Institute of Animal Health, for his assistance to use infected hamster materials and Dr. Iwakura, Institute for medical Science, Tokyo University, for his kind gift of anti-HIV P24 mAb TA8.1 and for many useful discussions. We also acknowledge Dr. Yuasa, a member of the Administrative Committee of the Japanese Red Cross Society, Dr. Okazaki, vice director, and Dr. Nishimura, one of our scientific colleagues in the institute, for their useful discussions and encouragement. We would also like to thank all our colleagues of the Japanese Red Cross Society for their encouragement and support.

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別紙様式第2-1

No. 24

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2008. 1. 11	該当なし	

一般的名称	(製造承認書に記載なし)	研究報告の公表状況		公表国
販売名(企業名)	合成血「日赤」(日本赤十字社) 照射合成血「日赤」(日本赤十字社) 合成血-LR「日赤」(日本赤十字社) 照射合成血-LR「日赤」(日本赤十字社)		ProMED 20080107-0087, 2008 Jan 7. 情報源:[1]UK National CJD Surveillance Unit, monthly statistics, 2007, 2008 Jan 7.	英国

研究報告の概要

○プリオン病最新情報
[1]英国CJDサーベイランスユニット—月次統計と2007年の合計
月次CJD統計—2008年1月7日時点
以下の数字は英国CJDサーベイランスユニットに報告されたCJD疑い症例数及び確定・可能性例の死亡数である。
内訳は以下の通り: vCJD患者:vCJD確定例における死亡患者:114名。vCJD可能性例における死亡患者(神経病理学的に未確定):48名。vCJD可能性例における死亡患者(神経病理学的診断を保留):1名。死亡患者総数:163名。vCJD患者-存命中:3名。vCJD確定例または可能性例総数:166名。2007年12月の月例統計以来、新たにvCJDと診断された患者はないが、存命中の患者数は1名減少した。このデータは英国におけるvCJD流行は減少しつつあるとする見解に一致する。死亡患者数のピークは2000年の28名であり、その後2001年に20名、2002年に17名、2003年に18名、2004年に9名、2005年に5名、2006年に5名、2007年に5名と減少している。
2007年における全ての型のCJD症例の報告数は111名であった。死亡例は47名が孤発性CJD、2名が医原性CJD、4名が家族性CJD、1名がGSS、5名がvCJDだった。

報告企業の意見	今後の対応
2008年1月7日の時点で、英国CJDサーベイランスユニットに報告されたvCJD確定例または可能性例総数は166名、2007年中の死亡患者数は5名であり、英国におけるvCJD流行は減少しつつあるとする見解に一致するとの報告である。なお、2007年1月の同報告ではvCJD確定例または可能性例総数165名、死亡患者総数158名であったことから、2007年中のvCJD新規発症患者は1名、死亡患者は5名である。	日本赤十字社は、vCJDの血液を介する感染防止の目的から、献血時に過去の海外渡航歴(旅行及び居住)を確認し、欧州36ヶ国に一定期間滞在したドナーを無期限に献血延期としている。また、英国滞在歴を有するvCJD患者が国内で発生したことから、平成17年6月1日より1980～96年に1日以上の英国滞在歴のある方からの献血を制限している。今後もCJD等プリオン病に関する新たな知見及び情報の収集に努める。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「日赤」
合成血-LR「日赤」
照射合成血-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

Back

Archive Number 20080107.0087
Published Date 07-JAN-2008
Subject PRO/AH/EDR> Prion disease update 2008 (02)

PRION DISEASE UPDATE 2008 (02)
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A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases
<http://www.isid.org>

[With the continuing decline of the number of cases of variant Creutzfeldt-Jacob disease (abbreviated previously as vCJD or CJD (new var.) in ProMED-mail) in the human population, it has been decided to broaden the scope of the occasional ProMED-mail reports to include other prion-related diseases. Data on vCJD cases from any part of the world are now included in these updates where appropriate, and other forms of CJD (sporadic, iatrogenic, familial, and GSS (Gerstmann-Straussler-Scheinker disease) are included also when they have some relevance to the incidence and etiology of vCJD. - Mod.CP]

In this update:
[1] UK: National CJD Surveillance Unit -- Monthly statistics & 2007 totals
[2] UK - New vCJD type
[3], [4], [5] vCJD in vitro assays

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[1] UK: National CJD Surveillance Unit -- Monthly statistics & 2007 totals
Date: Mon 7 Jan 2008
Source: UK National CJD Surveillance Unit, monthly statistics, 2007 [edited]
<http://www.cjd.ed.ac.uk/figures.htm>

Monthly Creutzfeldt-Jakob disease statistics -- as of 7 Jan 2008

These following figures show the number of suspect cases of CJD referred to the CJD surveillance unit in Edinburgh and the number of deaths of definite and probable variant Creutzfeldt-Jakob disease [abbreviated in ProMED-mail as CJD (new var.) or vCJD], the form of the disease thought to be linked to BSE (bovine spongiform encephalopathy).

Definite and probable vCJD cases in the UK as of 7 Jan 2008

Summary of vCJD cases -- deaths

Deaths from definite vCJD (confirmed): 114
Deaths from probable vCJD (without neuropathological confirmation): 48
Deaths from probable vCJD (neuropathological confirmation pending): 1
Number of deaths from definite or probable vCJD (as above): 163

Summary of vCJD cases -- alive

Number of probable vCJD cases still alive: 3

Total

Number of definite or probable vCJD (dead and alive): 166

These data indicate that there have been no new cases diagnosed during the past month, but the number of patients alive has decreased

by one.

These data are still consistent with the view that the vCJD outbreak in the UK is in decline (although the incidence curve may be developing a tail). The peak number of deaths was 28 in the year 2000, followed by 20 in 2001, 17 in 2002, 18 in 2003, 9 in 2004, 5 in 2005, 5 in 2006, and 5 in 2007.

Totals for all types of CJD cases in the year 2007

As of 31 Dec 2007 in the UK in the year 2007, there were 111 referrals, 47 deaths from sporadic CJD, 2 deaths from iatrogenic CJD, 4 deaths from familial CJD, one from GSS, and 5 deaths from vCJD.

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[2] UK - New vCJD type
Date: Mon 7 Jan 2008
Source: Arch Neurol. 2007 Dec; 64(12):1780-4 [edited]
<http://archneur.ama-assn.org/cgi/content/abstract/64/12/1780>

[Prion disease update 2008 (01) contained brief press reports of the identification of a new form of vCJD in a young female patient, homozygote V/V at codon 129 of the PrPSc gene. The Abstract of the scientific paper describing this observation is reproduced below. - Mod.CP]

Creutzfeldt-Jakob disease, prion protein gene codon 129V/, and a novel PrPSc type in a young British woman
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By Mead S, Joiner S, Desbruslais M, Beck JA, O'Donoghue M, Lantos P, Wadsworth JD, Collinge J. MRC Prion Unit and Department of Neurodegenerative Disease, Institute of Neurology, University College London, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK.

Background
Variant Creutzfeldt-Jakob disease (vCJD) is an acquired prion disease causally related to bovine spongiform encephalopathy that has occurred predominantly in young adults. All clinical cases studied have been methionine homozygotes at codon 129 of the prion protein gene (PRNP) with distinctive neuropathological findings and molecular strain type (PrPSc type 4). Modeling studies in transgenic mice suggest that other PRNP genotypes will also be susceptible to infection with bovine spongiform encephalopathy prions but may develop distinctive phenotypes.

Objective
To describe the histopathologic and molecular investigation in a young British woman with atypical sporadic CJD and valine homozygosity at PRNP codon 129.

Design
Case report, autopsy, and molecular analysis.

Setting
Specialist neurology referral center, together with the laboratory services of the MRC [Medical Research Council] Prion Unit.

Subject
Single hospitalized patient.

Main Outcome Measures
Autopsy findings and molecular investigation results.

Results
Autopsy findings were atypical of sporadic CJD, with marked gray and white matter degeneration and widespread prion protein (PrP) deposition. Lymphoreticular tissue was not available for analysis. Molecular analysis of PrPSc (the scrapie isoform of PrP) from cerebellar tissue demonstrated a novel PrPSc type similar to that

seen in vCJD (PrPSc type 4). However, this could be distinguished from the typical vCJD pattern by an altered protease cleavage site in the presence of the metal ion chelator EDTA.

Conclusions
Further studies will be required to characterize the prion strain seen in this patient and to investigate its etiologic relationship with bovine spongiform encephalopathy. This case illustrates the importance of molecular analysis of prion disease, including the use of EDTA to investigate the metal dependence of protease cleavage patterns of PrPSc.

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[The following 3 reports (3, 4, & 5), appearing during the past month (December 2007) describe new techniques for the in vitro assay of prions that promise to accelerate their characterization and epidemiology. - Mod.CP]

[3] vCJD in vitro assays
Date 11 Dec 2007
Source: PNAS, 26 Dec 2007, vol. 104, no. 52, 20908-20913 [edited]
<http://www.pnas.org/cgi/content/abstract/104/52/20908?etoc>

Prion strain discrimination in cell culture: The cell panel assay
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By Sukhvir P. Mahal*, Christopher A. Baker*, Cheryl A. Demczyk*, Emery W. Smith*, Christian Julius, and Charles Weissmann. At the Department of Infectology, Scripps Florida, 5353 Parkside Drive, Jupiter, FL 33458; and Institute of Neuropathology, University Hospital of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.

Abstract:
Prions are thought to consist mainly or entirely of misfolded PrP, a constitutively expressed host protein. Prions associated with the same PrP sequence may occur in the form of different strains; the strain phenotype is believed to be encoded by the conformation of the PrP. Some cell lines can be persistently infected by prions and, interestingly, show preference for certain strains. We report that a cloned murine neuroblastoma cell population, N2a-PK1, is highly heterogeneous in regard to its susceptibility to RML and 22L prions. Remarkably, sibling subclones may show very different relative susceptibilities to the 2 strains, indicating that the responses can vary independently. We have assembled 4 cell lines, N2a-PK1, N2a-R33, LD9 and CAD5, which show widely different responses to prion strains RML, 22L, 301C, and Me7, into a panel that allows their discrimination in vitro within 2 weeks using the standard scrapie cell assay (SSCA).

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[4] vCJD in vitro assays
Date: 20 Dec 2007
Source: Proc. Natl. Acad. Sci. USA, 10.1073/pnas.0710152105 [edited]
<http://www.pnas.org/cgi/content/abstract/0710152105v1?etoc>

Prion detection by an amyloid seeding assay

By David W. Colby, Qiang Zhang, Shuyi Wang, Darlene Groth, Giuseppe Legname, Detlev Riesner, and Stanley B. Prusiner. At the Institute for Neurodegenerative Diseases and Departments of Neurology and Biochemistry and Biophysics, University of California, San Francisco, CA 94143; and the Institut fur Physikalische Biologie, Heinrich-Heine Universitat, 40225 Dusseldorf, Germany.

Abstract:

Polymerization of recombinant prion protein (recPrP), which was produced in bacteria, into amyloid fibers was accompanied by the acquisition of prion infectivity. We report here that partially purified preparations of prions seed the polymerization of recPrP into amyloid as detected by a fluorescence shift in the dye Thioflavin T. Our amyloid seeding assay (ASA) detected PrPSc, the sole component of the prion, in brain samples from humans with sporadic Creutzfeldt-Jakob disease, as well as in rodents with experimental prion disease. The ASA detected a variety of prion strains passaged in both mice and hamsters. The sensitivity of the ASA varied with strain type; for hamster Sc237 prions, the limit of detection was approximately 1 fg. Some prion strains consist largely of protease-sensitive PrPSc (sPrPSc), and these strains were readily detected by ASA. Our studies show that the ASA provides an alternative methodology for detecting both sPrPSc and protease-resistant PrPSc that does not rely on protease digestion or immunodetection.

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[5] vCJD in vitro assays
Date: 9 Dec 2007
Source: Nature Neuroscience 11, 109 - 117 (2007) [edited]
<http://www.nature.com/neuro/journal/v11/n1/abs/nn2028.html>

A versatile prion replication assay in organotypic brain slices
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By Jeppe Falsig1, Christian Julius1, Ilan Margalith1, Petra Schwarz1, Frank L Heppner1,2 & Adriano Aguzzi. At the Institute of Neuropathology, University of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.

Abstract:
Methods enabling prion replication ex vivo are important for advancing prion studies. However, few such technologies exist, and many prion strains are not amenable to them. Here we describe a prion organotypic slice culture assay (POSCA) that allows prion amplification and titration ex vivo under conditions that closely resemble intracerebral infection. 35 days after contact with prions, mouse cerebellar slices had amplified the abnormal isoform of prion protein, PrPSc, >105-fold. This is quantitatively similar to amplification in vivo, but 5-fold faster. PrPSc accumulated predominantly in the molecular layer, as in infected mice. The POSCA detected replication of prion strains from disparate sources, including bovines and ovines, with variable detection efficiency. Pharmacogenetic ablation of microglia from POSCA slices led to a 15-fold increase in prion titers and PrPSc concentrations over those in microglia-containing slices, as well as an increase in susceptibility to infection. This suggests that the extensive microglial activation accompanying prion diseases represents an efficacious defensive reaction.

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[see also:
Prion disease update 2008 (01): correction 20080104.0046
Prion disease update 2008 (01) 20080102.0014
2007

Prion disease update 2007 (08) 20071205.3923
Prion disease update 2007 (07) 20071105.3602
Prion disease update 2007 (06) 20071003.3269
Prion disease update 2007 (05) 20070901.2879
Prion disease update 2007 (04) 20070806.2560
Prion disease update 2007 (03) 20070702.2112
Prion disease update 2007 (02) 20070604.1812
Prion disease update 2007 20070514.1542
CJD (new var.) update 2007 (05) 20070403.1130
CJD (new var.) update 2007 (04) 20070305.0780