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LETTER

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A recipient of immunoglobulin from a donor who developed vCJD

Dear Editor,

We present the case of a female patient who at the age of 61 years was diagnosed with common variable immunodeficiency (CVID) after having suffered recurrent pulmonary infections for 10 years. A delay in the diagnosis of antibody deficiency is unfortunately not uncommon [1]. She received intravenous immunoglobulin (IVIG) replacement therapy with three weekly infusions of Vigam (BPL, Hertfordshire, UK) from 1995 onwards. During the period January 1997 to February 1998 she received batches of immunoglobulin that contained plasma from a donor who later developed variant Creutzfeldt–Jakob disease (vCJD). She received 8 × 5 g vials from batch VGD 049 and 4 × 2·5 g vials from VGD 050. The estimated ID50/g of these batches were 0·0000112 and 0·0000688, respectively. At age 72, she died of recurrence of adenocarinoma of the bowel.

Post-mortem analysis of tissues was performed by the National Creutzfeldt-Jakob Disease Surveillance Unit. She had been embalmed after death, by the introduction of formaldehyde into her femoral artery, but this process is not known to affect the detection of prion material in the body tissues. Western blotting of spleen and lymph nodes was negative for prion protein. There was no evidence of prion protein being present in the brain on histological, immunocytochemical or Western blot analysis. The time interval between treatment with the implicated batches and death from unrelated causes was 9 years, which is longer than the interval from transfusion to death in the reported cases of vCJD transmission by red cell components (5–8·5 years) [2]. Therefore, it seems reasonable to expect to find evidence of abnormal prions if transmission had occurred in this case.

Although the patient received IVIG from a batch containing plasma from a donor who developed vCJD, the patient did not develop vCJD clinically, and there was no evidence of prion protein deposition using histopathological and molecular techniques. There are no known cases of prion transmission by IVIG, in contrast to transfusions of red cell components where four cases have been reported to date [2]. The safety of pooled plasma products such as IVIG has been enhanced by adding to their manufacturing scheme multiple steps that reduce the potential for such transmission. Current IVIG manufacturing schemes are able to remove prion particles with up to a 5 log reduction [3,4] such that the risk of transmission of vCJD by IVIG may be low, even when a donation contains prion protein.

Although there have been no reports of vCJD transmission by IVIG, UK plasma has not been used for fractionation of pooled plasma products since 1997 as a (continuing) precautionary measure to avoid possible transmission. There are many indications for the use of IVIG [5], and worldwide demand exceeds supply. More stringent indications for its use are currently being drawn up and implemented in the UK (http://www.ivig.nhs.uk). Increasing difficulty in UK supply from the world market suggests that it may be appropriate to re-examine whether the ban on the use of UK plasma to make fractionated pooled plasma products should continue. We believe that this case highlights many of the issues surrounding the current debate.

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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	総合機構処理欄
				2008. 12. 18	該当なし	

一般的名称	新鮮凍結人血漿	研究報告の公表状況		公表国
販売名(企業名)	新鮮凍結血漿「日赤」(日本赤十字社) 新鮮凍結血漿-LR「日赤」(日本赤十字社)		Watson R. BMJ 2008 Nov; 337(7680)	ベルギー

研究報告の概要

○クラミジアは2006年に欧州でもっとも多く報告された感染症であることが新しいデータで示された
欧州疾病管理予防センター(ECDC)の調査によると、クラミジア症は2006年に欧州において225,000件を上回る症例が記録され、もっとも報告頻度の高い感染疾患であった。以下、ランブル鞭毛虫症(193,000症例)、カンピロバクター症(180,000症例)、サルモネラ症(168,000症例)と続き、ストックホルム研究所に定期的に報告される47感染症のうちの上位10位を占めた他の感染症は、結核、流行性耳下腺炎、淋病、C型肝炎、侵襲性肺炎球菌疾患、HIVであった。
結核症例数はEU加盟27カ国とアイスランド、ノルウェー、リヒテンシュタインで減少傾向を示したが、英国、オランダ、スイス、ノルウェー、スウェーデンなどの移民では50%以上増加した。毎年、欧州では約90,000名が結核と診断され7,800名が死亡する。主に男性と性的な接触をもつ男性のHIV感染は増加し、毎年約30,000名がHIV / AIDSの診断を受け1,800名が死亡する。2010年までに欧州での根絶を目指している麻疹は6,279症例を記録している。
季節性インフルエンザは、年間2,500万人～5,000万人が感染し約40,000人が死亡する。また、欧州では毎年400万人ほどが院内感染し37,000名が死に至る。
メチシリン耐性黄色ブドウ球菌(MRSA)に関する状況は2002年以降ベルギー、オーストリアとスロベニアでは改善されたが、それ以外の国は横ばいまたは増加した。抗生物質の不適切な使用が公衆衛生における重大な脅威を招くこと、抗生物質の有効性を保つことは自身の責任であるとしたキャンペーンが展開されている。

報告企業の意見	今後の対応
欧州における2006年の感染症の発生報告はクラミジアが最も多く、以下、ランブル鞭毛虫症、カンピロバクター症、サルモネラ症、結核、流行性耳下腺炎、淋病、C型肝炎、侵襲性肺炎球菌疾患、HIVの順であったとの報告である。	今後も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

新鮮凍結血漿「日赤」
新鮮凍結血漿-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

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News

Chlamydia was most often reported infection in Europe in 2006, new data show

Rory Watson

[1] Brussels

Just over 225 000 cases of chlamsydia were recorded in Europe in 2006, making it the most frequently reported infectious disease, the latest research by the European Centre for Disease Prevention and Control shows.s

The findings, which will be published in the Stockholm based centre's annual epidemiological report in a few weeks' time, also confirm that giardiasis was the second commonest disease, with 193 000 cases. This is considerably more than the 15 000 reported in 2005, but the increase is almost entirely due to the 170 000 cases that occurred in Romania.

Two other food and waterborne infections came in third and fourth place: campylobacteriosis (180 000 cases) and salmonellosis (168 000). Other infectious diseases to feature in the top 10 of the 47 that are routinely reported to the Stockholm agency were tuberculosis, mumps, gonorrhoea, hepatitis C, invasive pneumococcal disease, and HIV.

Andrea Ammon, head of the centre's surveillance unit, gave an early presentation of the report's contents at a meeting of the agency's management board in Paris last week.

She noted that although the number of cases of tuberculosis had tended to fall in the 27 European Union members and in Iceland, Norway, and Liechtenstein, increases of up to 50% or more were being found among immigrants in countries such as the United Kingdom, the Netherlands, Switzerland, Norway, and Sweden.

The report also confirms an increase in infections of HIV, mainly among men who have sex with men, and records 6279 cases of measles, a disease that Europe is committed to eradicate by 2010.

The centre says that some four million people in Europe are infected every year while being treated in hospitals or clinics, of whom 37 000 die as a result. Seasonal flu affects between 25 and 50 million people a year, killing around 40 000.

Each year some 90 000 diagnoses of tuberculosis are made, a disease that kills 7800 people, while HIV or AIDS is identified in about 30 000 people, 1800 of whom die from the disease.

Although the situation regarding meticillin resistant *Staphylococcus aureus* (MRSA) had improved in Belgium, Austria, and Slovenia since 2002, in all other countries the levels of resistance to MRSA had either remained the same or grown. Data presented by Dominique Monnet, programme coordinator for antimicrobial resistance, showed that a threefold gap exists between countries that prescribe antibiotics to outpatients the most and those that do so the least.

Drawing on the high profile information campaigns that have helped to reduce use of antibiotics in France and Belgium, the Stockholm centre has helped more than 30 countries throughout Europe to run antibiotic awareness events in recent weeks. The common messages at the different events are that inappropriate use of antibiotics poses a serious threat to public health and that ensuring that antibiotics remain effective is everyone's responsibility.

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More information is at www.ecdc.europa.eu.

別紙様式第2-1

No. 5

医薬品 研究報告 調査報告書

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研究報告の概要

○FDAに報告された供血後及び輸血後の死亡例 2007年度概要

2005年度から2007年度にかけて米国食品医薬品局(FDA)に報告された供血後及び輸血後の死亡例の概要である。

2007年度に、FDAは受血者76件、供血者17件の死亡報告を受領した。受血者死亡例の内訳は、52件が輸血に関連したもの、11件が死亡原因として輸血を排除できないもの、13件が輸血と関連しないものであった。

過去3年間の合計は177例で、内訳はTRALIが98件(55%)で最も高く、微生物感染は21件(12%)であった。微生物感染の内5件(24%)をバベシア症が占め、ついで*Staphylococcus aureus*が4件(19%)となった。

アフェレーシス血小板に関連した致死性の微生物感染報告は、2005年度から2006年度にかけて減少が見られ、2007年度も低いままであった。

報告企業の意見	今後の対応
2005年度から2007年度にかけて米国食品医薬品局に報告された供血後及び輸血後の死亡例の概要である。	日本赤十字社では、薬事法及び関連法令に従い輸血副作用・感染症情報を収集し、医薬品医療機器総合機構を通じて国に報告している。今後も引き続き輸血副作用・感染症に関する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

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