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研究報告の概要

パルボウイルスPARV4は、ヒト宿主のパルボウイルス科の種類として最近記載された。
血中のPARV4の保有率を調査するため、定量的TaqMan PCRが開発され、様々な集団からのプラズマ、血清または全血について検討した。８つの検体がPARV4陽性であった（高いコピー数が１つ）。高力価陽性血漿は約 5 × 10^8genome equivalents/mLのウイルス量であった。間接免疫蛍光法でPARV4抗体陽性確認された２つのヒト血清が高力価ヒト血漿で自然のPARV4を視覚化する試みとして免疫電子顕微鏡に使用された。PARV4粒子はこれら２つの血清のうち１つで観察された。
我々の知る限りでは、自然のPARV4が可視化されたのはこれが初めてのことである。

報告企業の意見	今後の対応
ヒト血清でPARV4が免疫電子顕微鏡法により可視化された最初の報告である。 パルボウイルス４（PARV4）は、パルボウイルス科パルボウイルス亜科のどの属にも分類されないウイルスである。また、PARV4が発見されたのは2005年であり、PARV4及びその関連変異型であるPARV5の病原性は現時点では明らかではない。血漿分画製剤からの伝播事例は報告されていないが、英国で1970年代及び1980年代に製造された第Ⅷ因子製剤からPARV4が検出されている。万一、原料血漿にPARV4が混入した場合、 CPVをモデルウイルスとしたウイルスバリデーション試験成績からは、PARV4の製造工程における不活化・除去が十分であるとはいえないので、今後注意深く追加情報をフォローする必要があると考える。	PARV4 に関する追加情報の入手に努める。

使用上の注意記載状況・その他参考事項等

2. 重要な基本的注意
(2) 溶血性・失血性貧血の患者〔ヒトパルボウイルスB19の感染を起こす可能性を否定できない。感染した場合には、発熱と急激な貧血を伴う重篤な全身症状を起こすことがある。〕
(3) 免疫不全患者・免疫抑制状態の患者〔ヒトパルボウイルスB19の感染を起こす可能性を否定できない。感染した場合には、持続性の貧血を起こすことがある。〕
2. 重要な基本的注意
(1)略
1) 血漿分画製剤の現在の製造工程では、ヒトパルボウイルスB19等のウイルスを完全に不活化・除去することが困難であるため、本剤の投与によりその感染の可能性を否定できないので、投与後の経過を十分に観察すること。
5. 妊婦、産婦、授乳婦等への投与
妊婦又は妊娠している可能性のある婦人には、治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。〔妊娠中の投与に関する安全性は確立していない。本剤の投与によりヒトパルボウイルスB19の感染の可能性を否定できない。感染した場合には胎児への障害（流産、胎児水腫、胎児死亡）が起こる可能性がある。〕。

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Short Communication

Parvovirus PARV4 visualization and detection

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The parvovirus PARV4 is the most recently described member of the family *Parvoviridae* that has a human host. To investigate the prevalence of PARV4 in blood, a quantitative TaqMan PCR was developed and plasma, sera or whole blood from a variety of population groups were examined. Eight samples were positive for PARV4, one at high copy number. The high-titre-positive plasma had an approximate viral load of 5×10^8 genome equivalents ml^{-1}. Two human sera, identified as PARV4 antibody-positive by indirect immunofluorescence, were used in immune electron microscopy to try to visualize native PARV4 within the high-titre human plasma. PARV4 particles were observed using one of these two sera. To our knowledge, this is the first time that native PARV4 has been visualized.

PARV4 is the most recently described member of the family *Parvoviridae* that has a human host (Jones *et al.*, 2005). It is currently a virus without any apparent disease association (Fryer *et al.*, 2007a). It was identified by a random amplification of nucleic acids extracted from a patient with acute virus infection who was co-infected with hepatitis B virus (HBV) (Jones *et al.*, 2005). Two further genotypes of PARV4 have now been described (Fryer *et al.*, 2006; Simmonds *et al.*, 2008). Very little is known about PARV4 and its biology. It was initially described as 'not closely related to any known parvoviruses' (Jones *et al.*, 2005). However, further work has shown that PARV4 is most similar to the recently discovered bovine and porcine HoKo viruses (Lau *et al.*, 2008) and that it groups together with these and also the more distantly related Myanmar erythrovirus (Hijikata *et al.*, 2001), another porcine virus.

The human parvovirus B19 can be present at very high titres in the blood of infected individuals. Plasma and whole-blood samples thought likely to harbour PARV4, namely samples being tested for hepatitis B or C or from human immunodeficiency virus (HIV)-positive patients, were therefore examined. For comparison, samples from UK blood donors were also tested. All samples analysed were anonymized. The frequency of detection of PARV4 in the UK blood-donor population is expected to be low, based on limited data from previously reported surveys (Fryer *et al.*, 2007b; Simmonds *et al.*, 2007; Schneider *et al.*, 2008), although large, formal studies have yet to be performed.

Nucleic acid was extracted from plasma, serum or whole blood, either manually using Qiagen blood kit spin columns or on a Qiagen BioRobot. A quantitative TaqMan PCR (Q-PCR) was designed with the aid of Beacon Designer 3 software (Premier Biosoft International) and optimized for open reading frame (ORF) 2 of PARV4. The Q-PCR was performed on an ABI 7500 platform (Applied Biosystems), using ABgene reagents, and was shown to have linearity of detection over the range 10^1–10^8 copies ml^{-1}, with a limit of sensitivity of 50 copies ml^{-1}. An oligonucleotide positive control of the target sequence was synthesized (Eurofins MWG Operon), but was subsequently replaced by a biological standard: a high-titre-positive plasma, once one had been identified. Murine cytomegalovirus was used as an internal extraction and amplification control. Samples tested and results are shown in Table 1. Q-PCR conditions were 95 °C for 15 min followed by 45 cycles of 95 °C for 15 s, 60 °C for 60 s. The TaqMan primers used were PWTPARV4.1F (5′-CCTCTCCGAGTCCATTAGCAGA-3′; 1937–1958) and PWTPARV4.1R (5′-GCTCCATACCTTTCAGCAGTTTC-3′; 2069–2047). The TaqMan probe was PWTPARV4-probe (5′-FAM-CGCCGCCGAGGACACCAGACAGT-TAM-3′; 1961–1983). Sequences are numbered according to GenBank accession no. AY622943.

In total, PARV4 DNA was detected in eight samples. Quantification of PARV4 in samples was initially carried out against a $\log_{10}$ dilution series of the oligonucleotide positive control and subsequently against a high-titre-positive control PARV4 plasma (designated plasma 129). This plasma had a viral load of 5×10^8 DNA copies ml^{-1} and was from a hepatitis C virus (HCV) RNA-positive, HCV antibody-negative patient. Viral loads of all eight positive samples are shown in Table 2. The four samples that had a viral load $\geqslant$760 copies ml^{-1} were amplified successfully for sequencing, but those with viral loads of $\leqslant$285 failed to amplify. Three samples (129, 135 and 342)

Table 1. Samples tested for PARV4 by Q-PCR

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV-1, human immunodeficiency virus type 1; IVDU, intravenous drug user.

Population group tested	*n*	No. (%) PARV4-positive by Q-PCR
HCV antibody-negative, RNA-positive blood donors (HCV window phase)	94	3 (3.2)
Samples for routine HCV RNA testing	88	2 (2.3)
Samples for routine HBV DNA testing	140	2 (1.4)
HIV-1 proviral DNA-positive IVDUs	50	0*
Samples for routine HIV-1 RNA viral load testing	88	1 (1.1)*
UK blood donors – 20 pooled DNA extracts from 96 donors	–	0

*Overall detection frequency of 1 in 138 (0.7 %) in HIV-1-positive samples tested.

were amplified by using a semi-nested PCR to ORF2, initially with primers PARV4Seq1 (5′-CCGGAACC-TTCAAGTCAAGCCA-3′; 2465–2486) and PARV4Seq2 (5′-CCGCTCAAGGTCTGGTTCAACAA-3′; 3010–2988), followed by PARV4Seq1 and PARV4Seq3 (5′-CAAGG-TGGACTCCGACATCTGG-3′; 2954–2933). The resulting 490 bp fragments from these three samples were then sequenced with PARV4Seq1 and PARV4Seq3. All three were typed as PARV4 genotype 1. Sample 168 was also confirmed as PARV4 genotype 1 by sequencing with primers PVORF1F and PVORF1R (Fryer *et al.*, 2006). Sequence similarity was determined by using the FASTA program at http://www.ebi.ac.uk and searching the Viral Database.

For electron microscopy, 300 µl high-titre plasma 129 was centrifuged at 48 000 *g* for 45 min. The resultant pellet was resuspended in distilled water and stained with 1.5 % phosphotungstic acid (PTA), pH 6.6. Grids were examined in a Philips 420 transmission electron microscope fitted with an AMT XR60 digital imaging system. Parvovirus particles were not seen. Small, round, featureless virus particles, such as parvoviruses, however, can be extremely difficult to detect, particularly amongst the background debris of plasma or serum. Immune electron microscopy (IEM), a technique that has been employed successfully to detect other small viruses, including parvovirus B19 (Cossart *et al.*, 1975; Curry *et al.*, 2006), was used in a further attempt to visualize the native PARV4 particles. Two serum samples containing antibody to PARV4 had been identified in our laboratory on the basis of their reactivity in an indirect immunofluorescence test (R. P. Parry, unpublished data). These two antibody-positive sera were each mixed with an aliquot of high-titre plasma 129, incubated at room temperature for 1 h and centrifuged at 48 000 *g* for 45 min. Pellets were resuspended in distilled water and stained with 1.5 % PTA or 2 % methylamine tungstate, pH 6.6, and examined as described above. Parvovirus-like particles that had been aggregated into clumps by one of the sera were seen (Fig. 1a). The particles measured around 20–22 nm in diameter and were morphologically typical of parvoviruses. For comparison, recombinant PARV4 capsids expressed in *Sf*9 cells by baculovirus (PARV4 capsids provided by Dr Kevin E. Brown, Health Protection Agency) can be seen in Fig. 1(b). The recombinant capsids and the particles found in plasma 129 are similar in size and have the characteristic hexagonal appearance of parvoviruses. Stain has penetrated into several of the recombinant particles, as would be expected, whereas the particles from plasma 129 appear complete.

Table 2. Viral loads of PARV4-positive samples

Sample	Viral load (DNA copies ml^{-1})				
	PARV4	HCV	HCV genotype	HBV	HIV
129	5×10^8	2.70×10^3	2b		
135	760	1.22×10^6	3a		
168	4.6×10^3	1.05×10^5	3a		
A5	1	5.04×10^6			
C10	5	+		+	
342	3.4×10^3			+	+
490	170			+	
H10	285				+

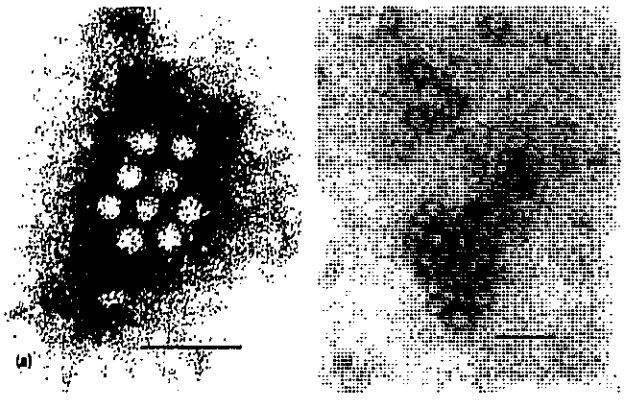

Fig. 1. Electron micrographs of parvovirus particles. (a) IEM of particles seen in plasma 129; antibody can be seen coating the particles. Stained with methylamine tungstate. (b) Recombinant viral capsids of PARV4, stained with PTA. Bars, 100 nm.

The antibody-aggregated clumps of particles observed in plasma 129 resembled the appearance of B19 virus when visualized by IEM. Plasma 129 and the two serum samples containing antibody to PARV4, however, were negative by PCR for B19 and human bocavirus, and it was concluded that the particles seen were PARV4.

Failure to detect virus particles with the second serum may have been related to the titre of the reagents. The sera were only tested at one dilution by immunofluorescence, but results from a prototype ELISA suggested that this second serum had a lower antibody titre to PARV4. For IEM purposes, the titre of PARV4 in plasma 129 was also low and probably near the limits of sensitivity for IEM detection. This may account for the fact that virus particles from this sample were not seen with PTA staining, rather than any difference between the stains.

PARV4 was detected at low frequency in samples from the blood of patients infected with HIV-1, HCV and HBV. In a study of the three human parvoviruses, B19, bocavirus and PARV4, in HIV-1-infected and non-infected individuals, Manning *et al.* (2007) established that a high proportion (70.8 %) of HIV-1-infected individuals harbour PARV4 in lymphoid and bone-marrow tissues, but none had viraemia. It is interesting to note that seven of the eight individuals in whom PARV4 was detected in the plasma were co-infected with hepatitis viruses (Table 1). The original discovery of PARV4 was in an intravenous drug user (IVDU) from the USA. The 94 HCV window-phase plasma samples analysed in our study for PARV4 were USA-sourced plasmas and the donors may have been remunerated financially. PARV4 was not detected in any of the UK blood donors tested.

These data contrast with those of a recent study in Thailand, which revealed PARV4 in sera both from IVDUs (8 %) and in blood donors (4 %) (Lurcharchaiwong *et al.*, 2008). Both of these figures are higher than those reported previously from the UK and elsewhere. It is again of interest that the majority of the PARV4-positive IVDUs in the Thai study, seven of eight (87.5 %), were HCV-co-infected; this may of course simply be coincidental, as the proportion of HCV positives within this group of IVDUs was very high (88.6 %). The determination of the prevalence of past infection with PARV4 in these different populations awaits the results of serological studies. Whether co-infection is a reflection of the natural history of the virus infection, a commonality of transmission routes or a consequence of underlying disease also awaits further elucidation.

The high viral load found in sample 129 (5×10^8 DNA copies ml^{-1}) suggests that this patient was experiencing active virus replication and may represent primary infection. The only other known high-level samples were from the original patient, which contained 6 $\log_{10}$ copies ml^{-1} (E. Delwart, personal communication), and from archived plasma pools with 6.58 $\log_{10}$ copies ml^{-1} (Fryer *et al.*, 2007b). It is not known whether the lower viral loads found in this (Table 2) and other studies represent virus replication, waning virus levels as antibody develops or a chronic virus carrier state. Fluctuating low levels of B19 DNA were observed in the plasma of 7.9 % of patients with congenital haemoglobinopathy. It has been postulated that this may be due to minor reactivation from sites of virus persistence (Lefrère *et al.*, 2005), which may also explain the 1 % of pregnant women (Lefrère *et al.*, 2005) and blood donors (Candotti *et al.*, 2004) who are B19 DNA-positive. A similar phenomenon may be occurring with PARV4. Further development of antibody assays and follow-up studies on PARV4-positive patients are required to investigate these hypotheses.

The high level of sequence conservation observed within the samples that tested positive for PARV4 is consistent with the findings of other groups. This argues for a recent evolutionary origin or a high conservation pressure. Manning *et al.* (2007) observed an apparent temporal shift in PARV4 genotypes, with genotype 1 representing the current 'modern' infection and genotype 2 the older strain. Study subjects positive for genotype 1 were all born after 1958 and those infected with genotype 2 were born between 1949 and 1956. A similar situation has recently been described for B19 variants, with genotype 1 superseding genotype 2 in the skin (Norja *et al.*, 2006). Demographic information on the patients and donors in our study was not available, as all samples were obtained in a random, anonymized manner.

The three genotypes of PARV4 now identified (Simmonds *et al.*, 2008) have not yet been related to any disease. However, 8 years elapsed between the discovery of B19 and its association with fifth disease (erythema infectiosum) (Anderson *et al.*, 1983). Our findings and those of others suggest that a parenteral transmission route is likely. It remains to be seen where PARV4 replicates and whether there are any disease associations.

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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
				2010. 7. 8	該当なし	

一般的名称	人血清アルブミン	研究報告の公表状況	Houfar MK, Mayr-Wohlfart U, Sireis W, Seifried E, Schrezenmeier H, Schmidt M. XXXIst International Congress of the ISBT; 2010 Jun 26-Jul 1; Berlin, Germany	公表国
販売名(企業名)	赤十字アルブミン20(日本赤十字社) 赤十字アルブミン25(日本赤十字社) 赤十字アルブミン20%静注4g/20mL(日本赤十字社) 赤十字アルブミン20%静注10g/50mL(日本赤十字社) 赤十字アルブミン25%静注12.5g/50mL(日本赤十字社)			ドイツ

研究報告の概要

○ヒトパルボウイルスB19(B19)DNA陽性血液製剤の感染性

背景:2000年以降、ドイツのウルム研究所では、B19に対する供血者NATスクリーニングを供血6～8週間後(すなわち血液製剤供給後)に実施している。本研究において、輸血された血液製剤中のウイルス濃度との関連においてB19陽性血液製剤の感染性を評価した。

研究方法:後方視的研究において、受血者を次の2群に分けた:A) B19ウイルス量≦10^5IU/mLの血液製剤受血者;B) B19ウイルス量＞10^5IU/mLの血液製剤受血者.

VP-1uゲノム領域の系統発生解析を、B19 DNA陽性供血者と受血者の対で実施した。また、すべての検体のIgM、IgG抗体を調べた。

結果:B19 DNAはB群の赤血球濃厚液受血者18名中9名に検出されたが、A群の受血者16名にはB19 DNAは検出されなかった(p=0.016)。系統発生解析では、供血者と受血者間で同一ゲノム配列を示した。

結論:血液製剤によるB19伝播は、ウイルス濃度と中和抗体価に相関することが分かった。

使用上の注意記載状況・その他参考事項等

赤十字アルブミン20
赤十字アルブミン25
赤十字アルブミン20%静注4g/20mL
赤十字アルブミン20%静注10g/50mL
赤十字アルブミン25%静注12.5g/50mL

血液を原料とすることに由来する感染症伝播等

報告企業の意見	今後の対応
輸血された血液製剤中のヒトパルボウイルスB19(B19)濃度と感染性について評価を行ったところ、B19伝播は、ウイルス濃度と中和抗体価に相関することが分かったとの報告である。 パルボウイルスB19は脂質膜のない小型DNAウイルスである。これまで本製剤によるB19感染の報告はない。B19は耐熱性とされていたが最近、液状加熱で容易に不活化できることが明らかにされた。本製剤の製造工程には、当該工程が含まれている。また最終製品についてB19-NAT陰性であることを確認していることから、本製剤の安全性は確保されている。	日本赤十字社では、以前よりRHA法によるB19抗原検査を導入しウイルス量の多い血液を排除してきた。2008年からさらに感度の高い化学発光酵素免疫測定法(CLEIA)を導入し、10^6IU/mL以上のB19を含む血液を陽性と判定し排除するものであることから、現在は原料血漿プール中のウイルス濃度が10^4IU/mL以下となっている。今後も輸血用血液及び血漿分画製剤の安全性向上のために努力する。

Materials: Test results of all blood samples from 929 RR blood donors recorded during the 2006–2009 period obtained at CITM by testing a total of 313,564 blood units were analyzed.
Results: In 929 RR donors, HCV predominated (51%) due to the use of combined anti HCV/HCV Ag-Ab test, followed by HIV (18.9%) and a comparable proportion of HBsAg and anti TP RR donors (14.4% and 15.8%, respectively). The HBsAg test yielded the highest rate of confirmed reactivity (42%), followed by syphilis-EIA (22.4%) and the lowest rate for HCV and HIV (4.4% and 1.1%, respectively). Table 1 summarizes the results of all RR donors analyzed during the study period, showing that 742 (79.9%) RR donors met the requirements for subsequent blood donation. In Table 2, next donations by these 742 donors are classified as follows: 475 (64%) presented for donation, 246 (51.8%) of them were seronegative and 229 (48.2%) showed repeat reactivity. Repeat reactivity was later recorded in 4 of 246 donors having continued with blood donation.

Table 1

2006-2009	HBV	HCV	HIV	SYPH.	Total	%
RR DONORS	134	473	175	147	929	100.0
Permanently deferred confirmed positive	56	21	2	33	112	12.0
Permanently deferred confirmed indetermined	3	28	2	9	42	4.5
Temporarily deferred/ To follow up	2	19	7	5	33	3.6
Free to donate/ Confirmed negative/flagged	73	405	164	100	742	79.9

Table 2

2006-2009	HBV	HCV	HIV	SYPH.	Total	%
Presented for donation	58	233	122	62	475	64.0
Next donations negative	33	119	65	29	246	51.8
Next donations reactive	25	1114	57	33	229	48.2

Conclusions: Testing for blood transmissible infections yielded nonspecific reactivity in the majority of 929 RR donors and repeat reactivity in nearly half of subjects (HBV 43%, HCV 48%, HIV 46% and syphilis 53%). None of RR donors developed infection (PCR negative) on follow up, whereas blood unit reactivity was recorded in 4 of 246 RR donors having continued with blood donation. Thus, the use of PCR on their reinclusion in the donor pool is justified. Further follow up in 229 blood donors scheduled for monitoring and additional testing resulted in permanent deferral in 108 and temporary deferral in 97 donors, whereas subsequent donation was approved in 24 donors.

P-0516

INFECTIVITY OF B19 DNA POSITIVE BLOOD PRODUCTS

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[1]German Red Cross, Institute Frankfurt, Frankfurt, Germany [2]Institute for Clinical Transfusion Medicine and Immunogenetics, German Red Cross, Ulm, Germany

Background: Since 2000, blood donor screening for B19 by NAT at the Ulm Institute has been conducted 6–8 weeks post donation, i.e. after transfusion of cellular blood products whereas at the Frankfurt Institute all donations are screened before releasing any blood product. In the current study, we evaluated the infectivity of B19 positive blood products in relation to the virus concentration in the transfused blood component.
Study design: In a retrospective study, recipients were classified into two groups (A: transfused with blood products with B19 virus load less than 10^5 IU/ml; B: transfused with blood products with B19 virus load $>10^5$ IU/ml). Phylogenetic analyses were done for B19 DNA positive donor and recipient pairs in the variant VP-1u genome region. All samples were investigated for IgM and IgG B19 antibodies.
Results: B19 DNA was detected in 9 out of 18 recipients of red blood cell concentrates from group B whereas none out of 16 recipients from group A were B19 DNA positive ($P = 0.016$). Phylogenetic analysis demonstrated identical genome sequences between donors and recipients.
Conclusions: B19 transmission by cellular blood products correlates with the virus concentration as well as with the concentration of neutralizing antibodies. As a consequence, blood donor screening for B19 by mini-pool NAT should be implemented for all products in order to discard all donations with a high virus burden and to enable transfusion of B19 negative blood products for at-risk patients.

P-0517

WHO WORKSHOPS ON DEVELOPING NATIONAL SYSTEMS FOR 100% QUALITY-ASSURED SCREENING OF BLOOD DONATIONS FOR TRANSFUSION-TRANSMISSIBLE INFECTIONS

Abu Amin N, Dhingra N

World Health Organization, Geneva, Switzerland

Background: The provision of safe blood and blood products for transfusion or manufacturing use involves a number of processes, from the selection of blood donors and the collection, processing and testing of blood donations to its administration to patients. There is a risk of error in each process in this "transfusion chain"which can have serious implications for transfused patients. Thus, while blood transfusion can be life-saving, there are associated risks, particularly the transmission of bloodborne infections. It is the responsibility of governments to assure a safe and sufficient supply of blood and blood products for all patients requiring transfusion. However, in 2007, 41 countries are not able to screen all blood donations for one or more of the transfusion-transmissible infections (TTIs) – including HIV, hepatitis B, hepatitis C and syphilis.
Aim: The main aims of the WHO workshops are to: provide an opportunity for the sharing of experience among countries on the challenges and strategies in developing national systems for quality-assured blood screening; identify needs and areas of concern in strengthening national blood screening programmes; develop country action plans for priority activities for national blood screening programmes, and make recommendations to international organizations for supporting countries to meet their needs in achieving 100% quality-assured screening of donated blood.
Methods: WHO Blood Transfusion Safety Programme had organized two 3-day workshop on "Developing National Systems for 100% Quality-Assured Screening of Donated Blood for Transfusion-Transmissible Infections". The WHO document, "Recommendations on Screening Donated Blood for Transfusion-Transmissible Infections" were used as the basis of the training workshop.
Results: Sixty participants from 25 countries in the African, South-East Asian and Western Pacific regions attended the workshops. These represent the countries that were not able to screen all donated blood for major transfusion-transmissible infections or to perform screening within a quality system. Invited participants from each country will include the national blood programme manager and a senior laboratory manager in the blood transfusion service (medical/scientific/technical) who is involved in setting up national systems for the quality-assured screening of donated blood. The working methodology of the workshop will include country presentations, group work and the development of country plans.
Conclusions: The workshops were able to facilitate the sharing of experience among countries on the challenges and strategies in developing national systems for quality-assured blood screening; identify variations in screening strategies, practices and areas of concern of the countries; provide opportunity for participants to develop country action plans for priority activities to strengthen national blood screening programmes, and strengthen the strategies and capacity of international organizations and institutions to respond to countries' needs on policy and technical guidance in supporting countries to meet their needs in achieving 100% quality-assured screening of donated blood.

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
				2010. 5. 7	該当なし	

一般的名称	人血清アルブミン	研究報告の公表状況		公表国
販売名(企業名)	赤十字アルブミン20(日本赤十字社) 赤十字アルブミン25(日本赤十字社) 赤十字アルブミン20%静注4g/20mL(日本赤十字社) 赤十字アルブミン20%静注10g/50mL(日本赤十字社) 赤十字アルブミン25%静注12.5g/50mL(日本赤十字社)		BID Jnl. Vol.16 No.5	米国

研究報告の概要

○ヒトスジシマカにおけるLa Crosseウイルス(LACV)(2009年米国テキサス州ダラス)
2009年8月にテキサス州ダラスで採取した、ヒトスジシマカにおけるLACVについて報告する。LACVは主にAedes triseriatusが媒介する、北アメリカでの小児脳炎の主要な原因である。しかし近年、LACV脳炎が南東部地域で増加し、南部でも報告されている。同時にアジアからの外来種であるヒトスジシマカが増加しているが、今までヒトスジシマカとLACV伝播の関連は不明であった。今回の調査で、テキサス州ダラスで採取したヒトスジシマカからLACVが検出された。これまで流行が確認されていた範囲外で、外来性の蚊に当該ウイルスが認められたことは、公衆衛生上の懸念である。

報告企業の意見	今後の対応
2009年8月にテキサス州ダラスで採取した、外来種であるヒトスジシマカからLa Crosseウイルスが検出されたとの報告である。 La Crosseウイルスはブニヤウイルス科の脂質膜を持つRNAウイルスである。これまで、本製剤によるLa Crosseウイルス感染の報告はない。本製剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれていることから、本製剤の安全性は確保されていると考える。	日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国(入国)後4週間は献血不適としている。また、発熱などの体調不良者を献血不適としている。今後も引き続き、新興・再興感染症の発生状況等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

赤十字アルブミン20
赤十字アルブミン25
赤十字アルブミン20%静注4g/20mL
赤十字アルブミン20%静注10g/50mL
赤十字アルブミン25%静注12.5g/50mL

血液を原料とすることに由来する感染症伝播等

La Crosse Virus in *Aedes albopictus* Mosquitoes, Texas, USA, 2009

Amy J. Lambert, Carol D. Blair, Mary D'Anton, Winnann Ewing, Michelle Harborth, Robyn Seiferth, Jeannie Xiang, and Robert S. Lanciotti

We report the arthropod-borne pediatric encephalitic agent La Crosse virus in *Aedes albopictus* mosquitoes collected in Dallas County, Texas, USA, in August 2009. The presence of this virus in an invasive vector species within a region that lies outside the virus's historically recognized geographic range is of public health concern.

La Crosse virus (LACV) is the most common cause of arthropod-borne, pediatric encephalitis in North America. A member of the California serogroup within the family *Bunyaviridae* and the genus *Orthobunyavirus*, LACV is enveloped and contains a negative-sense, tripartite genome with segments designated small (S), medium (M), and large (L). Cases of LACV-associated encephalitis, which can be fatal, occur within the geographic range of its principal vector, *Aedes triseriatus* mosquitoes. This native tree-hole breeding mosquito is distributed throughout wooded regions east of the Rocky Mountains within the United States. Historically, most LACV-associated encephalitis cases have occurred in upper midwestern states, including Wisconsin, Illinois, Minnesota, Indiana, and Ohio (Figure 1). In recent years, LACV encephalitis activity has increased above endemic levels in regions of the southeastern United States, including West Virginia, North Carolina, and Tennessee (Figure 1) (*1*). In addition, recent cases of LACV encephalitis have been reported as far south as Louisiana, Alabama, Georgia, and Florida (Figure 1).

Ae. albopictus is an invasive mosquito species that was first discovered in Houston, Texas, in 1985 (*2*); having apparently arrived in the United States in a shipment of used tires from Asia (*3*). An opportunistic container-breeder, its vector competence for many arthropod-borne viruses (arboviruses), including LACV, and its catholic feeding habit have made the invasion of *Ae. albopictus* mosquitoes disconcerting to researchers, who have warned of the potential for an increased incidence of vector-borne diseases as a result (*4*,*5*). Since 1985, the geographic distribution of these mosquitoes has grown to include most of the southeastern United States. The concurrent increase in LACV encephalitis activity has led to speculation on the possible transmission of LACV by *Ae. albopictus* mosquitoes as an accessory mechanism to the historically recognized transmission by *Ae. triseriatus* mosquitoes (*6*). LACV has been isolated from *Ae. albopictus* mosquitoes in Tennessee and North Carolina in 1999 and 2000, respectively, during a period of greatly increased LACV activity in those areas (*6*). However, the role of this species in LACV transmission remains unknown.

We report the isolation of LACV from a pool of 3 *Ae. albopictus* mosquitoes collected outside the known geographic range of the virus, in Dallas County, Texas, on August 13, 2009 (Figure 1). This is one of only several isolations of LACV within the state; the first isolate was derived from a pool of *Ae. infirmatus* mosquitoes collected in Houston in 1970 (*7*). After the identification of LACV in the Dallas pool, an additional isolation of LACV was made from a mixed pool of 29 *Ae. albopictus* and 2 *Ae. triseriatus* mosquitoes collected in Fort Bend County, Texas, in October 2009 (Figure 1). The Fort Bend County location is relatively near the site of collection of the 1970 Texas

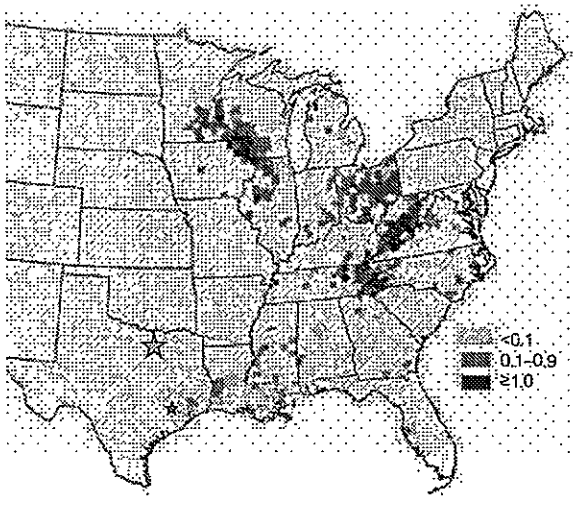

Figure 1. Geographic distribution of La Crosse virus (LACV) in accordance with the habitat range of *Aedes triseriatus* mosquitoes in the United States as inferred from the California serogroup virus neuroinvasive disease average annual incidence by county, 1996–2008. Incidence rates are shown in shades of blue. Dallas County and Fort Bend County locations of the 2009 LACV isolations from pools containing *Ae.albopictus* and *Ae. triseriatus* mosquitoes are indicated by green and red stars, respectively. Data and figure adapted from the Centers for Disease Control and Prevention website (www.cdc.gov/lac/tech/epi.html).

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LACV-positive pool and the known geographic distribution of LACV activity in southeastern Texas and Louisiana (Figure 1). Taken together, our results represent an unprecedented number of LACV findings within the state of Texas.

The Study

As part of ongoing arbovirus surveillance efforts, the City of Dallas Vector Control Division collected 65 mosquitoes in a gravid trap at the edge of a wooded area near a residential district in Dallas County on August 13, 2009. Upon their receipt at the Texas State Department of Health Services, none of the mosquitoes was viable. The mosquitoes were sorted and identified by sex. Female mosquitoes were grouped into 3 pools by species: pool no. AR6318, consisting of 50 *Culex quinquefasciatus* mosquitoes, pool no. AR6319, consisting of 3 *Ae. albopictus* mosquitoes; and pool no. AR6320, consisting of 1 *Ae. triseriatus* mosquito.

Generated pools were macerated in 1.5 mL of bovine albumin diluent arbovirus medium followed by 2 rounds of centrifugation at 10,000 rpm for 5 min each. Between each round of centrifugation, a rest period of 15 min was used to facilitate pellet formation. After centrifugation, 50 µL of the resultant supernatant was injected onto BHK and Vero cells. These cells were incubated at 37°C and examined for cytopathic effect (CPE) over the next 10 days. At day 5 postinoculation, Vero cells inoculated with the supernatant derived from pool no. AR6319 (*Ae. albopictus*) demonstrated marked CPE. This condition represented a preliminary virus isolation-positive result. No CPE was observed in the BHK cells. Infected cells were then subjected to immunofluorescent antibody assays with antibodies directed against various arboviruses, followed by the use of fluorescein isothiocyanate–conjugated antimouse antibodies for detection. From these analyses, the isolate derived from pool no. AR6319 (*Ae. albopictus*) was determined to be a California serogroup virus. Furthermore, pool no. 6318 (*Cx. quinquefasciatus*) tested positive for West Nile virus, and pool no. 6320 (*Ae. triseriatus*) was negative for virus by the above described methods.

To further identify the California serogroup virus identified in pool no. AR6319 (*Ae. albopictus*), the pool and the Vero cell–derived isolate were sent to the Centers for Disease Control and Prevention in Fort Collins, CO, USA, for additional testing. Upon receipt of the samples in Fort Collins, a reverse transcription–PCR was performed to amplify cDNAs from all 3 segments of the orthobunyavirus genome by using the consensus oligonucleotide primers shown in the Table and conditions and methods previously described (*8*). Generated cDNAs were then subjected to nucleotide sequencing and BLAST (www.ncbi.nlm.nih.gov/BLAST) analyses; the results indicated that the pool and the isolate were positive for LACV S, M, and L segment RNAs.

Subsequently, a pool (AR8973) of 29 *Ae. albopictus* and 2 *Ae. triseriatus* mosquitoes collected in Fort Bend County, Texas on October 5, 2009, was identified as positive for LACV S, M, and L segment RNAs by using the same processing and characterization methods described above. After these analyses, full-length S, M, and L segment genomic sequences (GenBank accession nos. GU591164–9) were generated for LACV RNAs extracted from LACV-positive pools and Vero cell isolates by using oligonucleotide primers specific for the previously published LACV prototype genome (human 1960, GenBank accession nos. EF485030–2) and methods previously described (*9*).

Phylogenetic analyses of partial LACV M segment sequences (Figure 2) indicate that the LACVs present in the Texas 2009 pools are closely related to LACVs isolated from Alabama, Georgia, and New York of the previously described lineage 2 (*11*) and genotype C (*7*) designations. These findings suggest a likely southeastern ancestry for the Texas 2009 LACV isolates.

Conclusions

The presence of LACV in *Ae. albopictus* mosquitoes in Dallas County, Texas, in late summer 2009 represents the possible expansion of the geographic range of an endemic pathogen within this invasive mosquito species in the United States. The subsequent occurrence of LACV in Fort Bend County in October 2009 should be of concern to public health practitioners who have been alerted to the

Table. Orthobunyavirus consensus oligonucleotide primers used for amplification and sequencing of La Crosse virus partial S, M, and L segment cDNAs, Texas, 2009*

Targeted genomic regions	Name	Primer sequence (5′ → 3′)	Approximate amplicon size, bp
S segment nucleocapsid ORF	Cal S forward	GCAAATGGATTTGATCCTGATGCAG	210
	Cal S reverse	TTGTTCCTGTTTGCTGGAAAATGAT	
M segment 5′ terminus/glycoprotein ORF	Ortho M 5′ terminus	AGTAGTGTACTACC	410
	Ortho M ORF reverse	TTRAARCADGCATGGAA	
L segment 5′ terminus/polymerase ORF	Ortho L 5′ terminus	AGTAGTGTACTCCTA	550
	Ortho L ORF reverse	AATTCYTCATCATCA	

*Oligonucleotide primers designed against conserved regions of the orthobunyavirus genome. S segment primers appear in a previous publication (*8*). All primers were applied in singleplex reactions using methods described previously (*8*) with altered primer annealing conditions of 50°C for 1 min. S, small; M, medium; L, large; ORF, open reading frame.

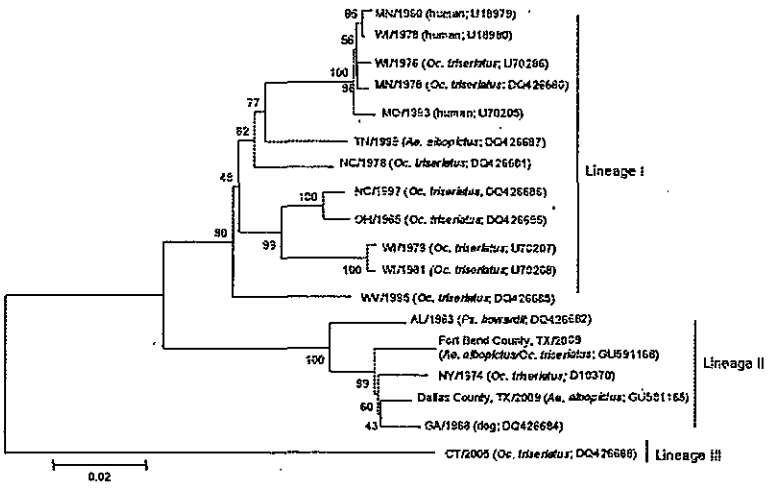

Figure 2. Phylogeny of La Crosse virus (LACV) medium (M) segment sequences of diverse origins. According to a limited availability of full-length sequences in GenBank, 1,663 nt of the M segment glycoprotein gene open-reading frame are compared. Isolate source and GenBank accession nos. appear after the isolate designation for each taxon. Sequences were aligned by ClustalW (*10*) and neighbor-joining and maximum-parsimony trees were generated by using 2,000 bootstrap replicates with MEGA version 4 software (*10*). Highly similar topologies and confidence values were derived by all methods and a neighbor-joining tree is shown. Scale bar represents the number of nucleotide substitutions per site. The 2009 Texas (TX) isolates group with strong support with lineage 2 viruses of the extreme south and New York (NY), which suggests a likely southern origin for LACV isolates. MN, Minnesota; WI, Wisconsin; Oc., *Ochlerotatus*; MO, Missouri; TN, Tennessee; *Ae.*, *Aedes*; NC, North Carolina; OH, Ohio; WV, West Virginia; AL, Alabama; *Ps.*, *psorophora*; GA, Georgia; CT, Connecticut.

presence of this pathogen near 2 major urban centers, Dallas and Houston. Of interest, San Angelo virus, which is serologically related to LACV, is known to occur in Texas and has been shown to replicate in and be transovarially transmitted by *Ae. albopictus* mosquitoes (*12*), although this virus has no known association with human disease. Cocirculation enables possible reassortment of genomic segments between LAGV and San Angelo virus, a phenomenon that has been described for viruses of the California serogroup within *Ae. albopictus* mosquitoes (*13*) with unknown public health outcomes.

Ms Lambert is a research microbiologist at the Centers for Disease Control and Prevention, Division of Vector-Borne Infectious Diseases, Fort Collins, Colorado. Her primary research interests lie in the molecular characterization, detection, and evolution of viruses of the family *Bunyaviridae*.

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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
				2010. 7. 8	該当なし	

一般的名称	人血清アルブミン	研究報告の公表状況		公表国
販売名(企業名)	赤十字アルブミン20(日本赤十字社) 赤十字アルブミン25(日本赤十字社) 赤十字アルブミン20%静注4g/20mL(日本赤十字社) 赤十字アルブミン20%静注10g/50mL(日本赤十字社) 赤十字アルブミン25%静注12.5g/50mL(日本赤十字社)		MMWR Vol. 59 No. 25	米国

研究報告の概要

○2009年の米国におけるウエストナイルウイルス(WNV)の流行状況
米国疾病管理予防センター(CDC)が発表した2009年の米国におけるWNVの流行状況である。米国の38州の262郡と、コロンビア特別区から720症例のWNV感染症が報告された。そのうち386例(54%)が神経侵襲性疾患で、334例(46%)が非神経侵襲性疾患であった。WNV感染症での死亡者は全部で33人が報告され、そのうち32人が神経侵襲性疾患であった。神経侵襲性疾患のうち229例(59%)が脳炎、117例(30%)が髄膜炎、40例(10%)が急性弛緩性麻痺であった。急性弛緩性麻痺40例のうち、27例(68%)が脳炎または髄膜炎を併発した。

使用上の注意記載状況・その他参考事項等

赤十字アルブミン20
赤十字アルブミン25
赤十字アルブミン20%静注4g/20mL
赤十字アルブミン20%静注10g/50mL
赤十字アルブミン25%静注12.5g/50mL

血液を原料とすることに由来する感染症伝播等

報告企業の意見	今後の対応
2009年、米国におけるウエストナイルウイルス感染症例は38州及びコロンビア特別区から720症例が報告され、そのうち386例が神経侵襲性疾患であり、全体の死者は33人であったとの報告である。 ウエストナイルウイルスは脂質膜を持つRNAウイルスである。これまで、本剤によるウエストナイルウイルス感染の報告はない。本剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれていることから、本剤の安全性は確保されていると考える。	日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国(入国)後4週間は献血不適としている。また、ウエストナイルウイルス感染の国内発生に備え、平成17年10月25日付血液対策課発事務連絡に基づき緊急対応の準備を進めているほか、厚生労働科学研究「献血血の安全性確保と安定供給のための新興感染症等に対する検査スクリーニング法等の開発と献血制限に関する研究」班と共同して対応について検討している。今後も引き続き情報の収集に努める。

(12)

Centers for Disease Control and Prevention
MMWR Morbidity and Mortality Weekly Report
Weekly / Vol. 59 / No. 25 July 2, 2010

West Nile Virus Activity — United States, 2009

West Nile virus (WNV) was first detected in the Western Hemisphere in 1999 in New York City and has since caused seasonal epidemics of febrile illness and neurologic disease across the United States, where it is now the leading cause of arboviral encephalitis (*1*). This report updates a previous report (*2*) and summarizes WNV activity in the United States reported to CDC in 2009. A total of 38 states and the District of Columbia (DC) reported 720 cases of WNV disease. Of these, 33 states and DC reported 386 cases of WNV neuroinvasive disease, for an incidence of 0.13 per 100,000 population. The five states with the highest incidence of WNV neuroinvasive disease were Mississippi (1.05 per 100,000), South Dakota (0.74), Wyoming (0.73), Colorado (0.72), and Nebraska (0.61). Neuroinvasive disease incidence increased with increasing age, with the highest incidence among persons aged ≥70 years. A total of 33 WNV deaths were reported, 32 from neuroinvasive disease. Calculating from the number of neuroinvasive disease cases and projections from 1999 serosurvey data, CDC estimated that 54,000 persons were infected with WNV in 2009, of whom 10,000 developed nonneuroinvasive WNV disease. The continuing disease burden caused by WNV affirms the need for ongoing surveillance, mosquito control, promotion of personal protection from mosquito bites, and research into additional prevention strategies.

WNV is a nationally notifiable disease. Data are reported to CDC through ArboNET, an Internet-based arbovirus surveillance system managed by state health departments and CDC (*2*). Using standard case definitions,* human WNV disease cases are classified as WNV neuroinvasive disease (e.g., meningitis, encephalitis, or acute flaccid paralysis) or WNV nonneuroinvasive disease (e.g., acute systemic febrile illness that often includes headache, myalgia, or arthralgia). Nonneuroinvasive disease reporting varies greatly by jurisdiction, depending on disease awareness, health-care–seeking behaviors, and testing practices. Therefore, this report focuses on WNV neuroinvasive disease cases, which are thought to be identified and reported more consistently because of the severity of the illness. In addition to human disease cases, ArboNET captures data on presumptively viremic blood donors (PVDs), veterinary cases, and WNV infections in sentinel animals (most commonly chickens), dead birds, and mosquitoes. Not all jurisdictions conduct nonhuman surveillance.

*Available at http://www.cdc.gov/ncphi/disss/nndss/casedef/arboviral_current.htm.

Human Surveillance

During 2009, a total of 720 cases of WNV disease were reported from 262 counties in 38 states and DC. Of these 720 cases, 386 (54%) were reported as WNV neuroinvasive disease and 334 (46%) as nonneuroinvasive disease. A total of 116 PVDs, identified through routine screening of the blood supply, also were reported. Of these PVDs, 92 (79%) were asymptomatic, 23 (20%) developed nonneuroinvasive disease, and one (1%) subsequently developed neuroinvasive disease. PVDs who developed symptomatic disease were included in disease case counts.

The 386 reported cases of neuroinvasive disease represented a rate of 0.13 per 100,000 population in the United States, based on July 1, 2009 U.S. Census population estimates (Figure 1). States reporting the most WNV neuroinvasive disease cases were Texas with 93 (24% of U.S. cases) and California with 67 (17%). Washington, which reported only two neuroinvasive disease cases in 2008, reported 26 (7%) cases in 2009. The five states with the highest incidence were Mississippi (31 cases,

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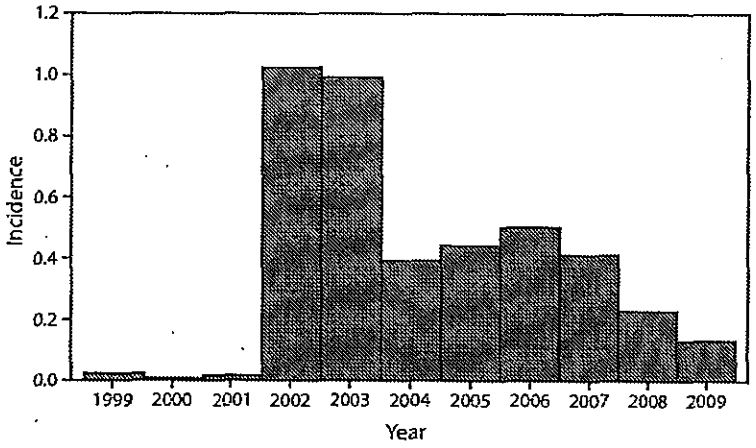
FIGURE 1. Annual incidence* of cases of West Nile virus neuroinvasive disease† — ArboNET, United States, 1999–2009§

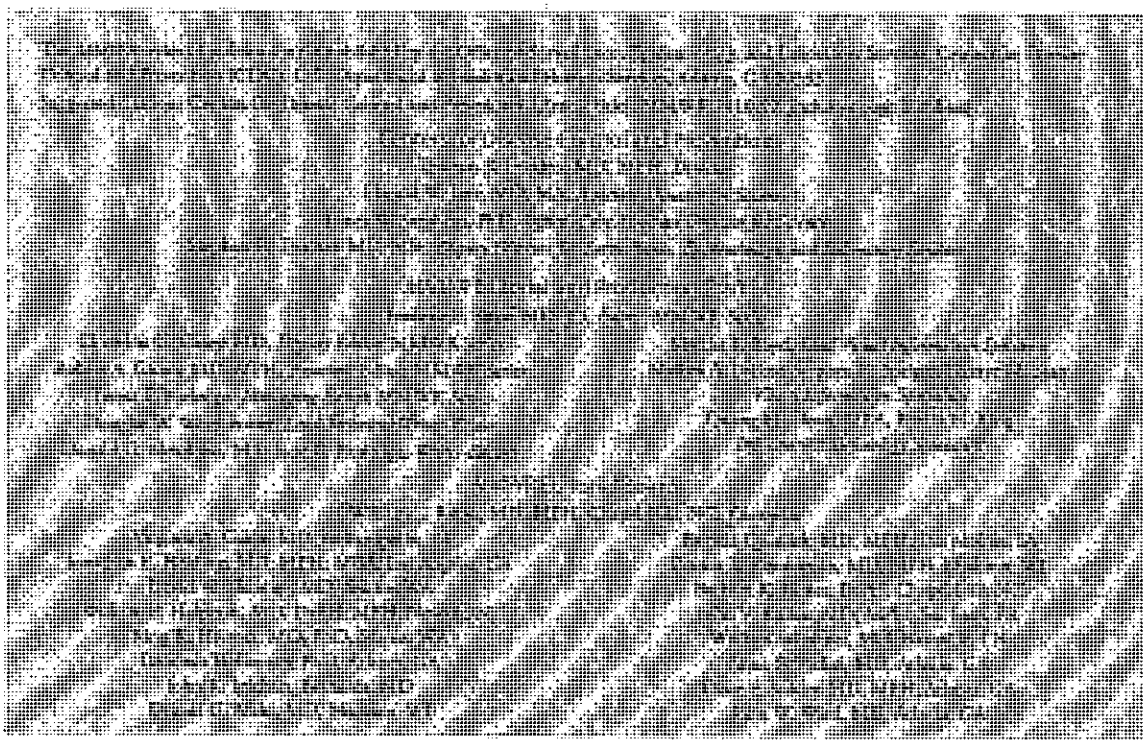


*Per 100,000 population, based on July 1 U.S. Census estimates for each year.
†Meningitis, encephalitis, or acute flaccid paralysis.
§N = 12,208 during 1999–2009; N = 386 in 2009

1.05 cases per 100,000 residents), South Dakota (six cases, 0.74), Wyoming (four cases, 0.73), Colorado (36 cases, 0.72), and Nebraska (11 cases, 0.61) (Figure 2). WNV neuroinvasive disease peaked in the United States during mid-August, and 352 (91%) of the 386 cases were reported during July–September. This seasonality was consistent with trends observed over the preceding 10 years (*2*).

Of the 386 neuroinvasive disease cases, 226 (59%) occurred in males. The median age of patients was 60 years (range: 2–91 years), with increasing incidence among persons in older age groups (Figure 3). Overall, 368 (95%) patients with neuroinvasive disease were hospitalized, and 32 (8.3%) died (median age: 72 years; range: 19–89 years). A total of 229 (59%) neuroinvasive disease cases were classified as encephalitis, 117 (30%) as meningitis, and 40 (10%) as acute flaccid paralysis; 27 (68%) of the 40 cases classified as acute flaccid paralysis had coincident encephalitis or meningitis.

Serologic surveys indicate that for every case of WNV neuroinvasive disease there are approximately 140 infections and approximately 20% of infected persons develop nonneuroinvasive disease (*3*). Using the 386 reported neuroinvasive disease cases, CDC estimated that 54,000 infections and 10,000 cases of WNV nonneuroinvasive disease occurred in the United States in 2009. Only 334 nonneuroinvasive disease cases were reported to ArboNET in 2009, representing approximately 3% of the estimated number.



Animal Surveillance

Of 298 reported veterinary cases of WNV disease, 275 (92%) occurred in equines and 23 (8%) occurred in other species: squirrels, 13; canines, eight; camelids, one; and deer, one. The equine cases were reported from 168 counties in 36 states, with 72 (26%) reported from Washington. The number of reported WNV-infected equines peaked during the first week of September.

In 2009, a total of 759 dead WNV-infected birds were reported from 141 counties in 25 states and the District of Columbia; California reported 515 (68%) dead birds. Of the 141 counties reporting WNV-infected birds, 92 (65%) counties in 19 states reported infected dead birds but no human disease cases. The number of reported WNV-infected birds peaked during the first week of September. Corvids (e.g., crows, jays, and magpies), which are targeted for surveillance by most states, accounted for 534 (70%) of the birds. Since 1999, WNV infection has been reported in 328 avian species, including two species, MacGillivray's warbler and tricolored blackbird, in which WNV was identified for the first time during 2009.

Mosquito Surveillance

In 2009, a total of 6,646 mosquito pools[†] from 351 counties in 40 states and DC were reported as testing positive for WNV. Among the WNV-positive pools, 4,987 (75%) had species of *Culex* mosquitoes thought to be the principal vectors of WNV (e.g., *Culex pipiens*, *Culex quinquefasciatus*, *Culex restuans*, *Culex salinarius*, and *Culex tarsalis*). Unidentified or other species of *Culex* mosquitoes made up 1,488 (22%) pools, and non-*Culex* mosquito species (e.g., *Aedes* sp., *Anopheles* sp., *Coquillettidia perturbans*, *Culiseta* sp., *Mansonia titillans*, *Psorophora columbiae*, and *Uranotaenia sapphirina*) made up 171 (3%) pools. Data from 2009 also included the first report of WNV infection in *Aedes epactius*, which was collected in Texas. The number of reported WNV-infected mosquito pools peaked during mid-August.

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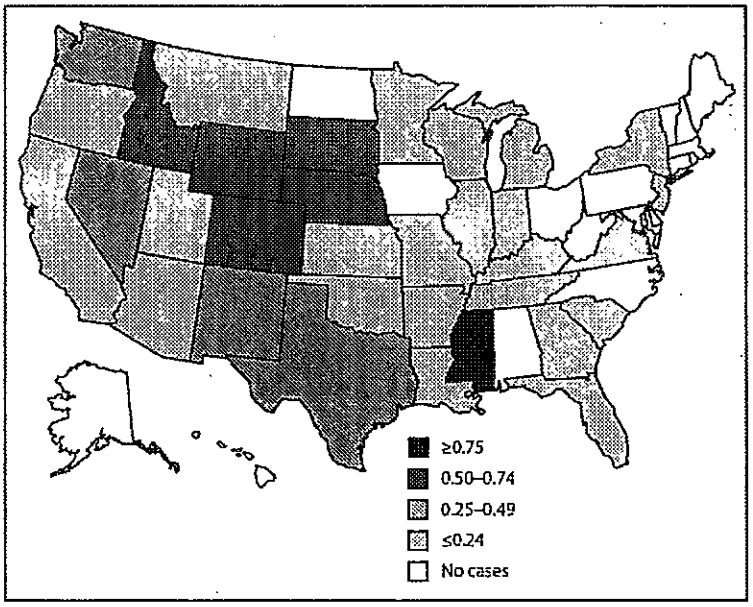
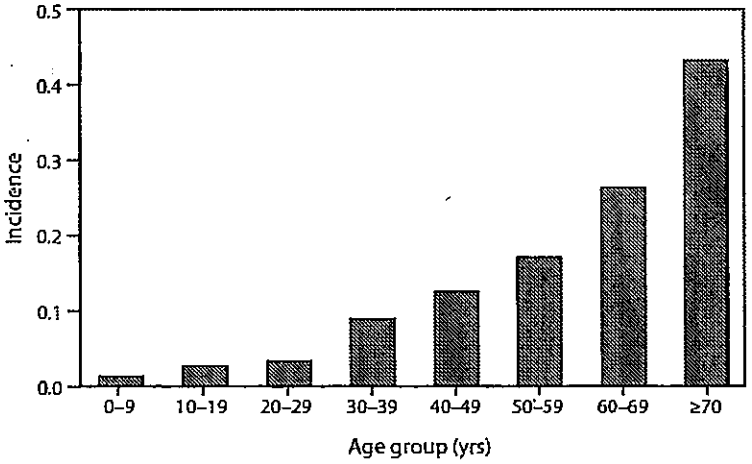
[†] A sample of mosquitoes (usually no more than 50) of the same species and sex, collected within a defined sampling area and period.

FIGURE 2. Incidence* of cases (N = 386) of West Nile virus neuroinvasive disease† — ArboNET, United States, 2009



* Per 100,000 population, based on July 1, 2009 U.S. Census estimates.
† Meningitis, encephalitis, or acute flaccid paralysis.

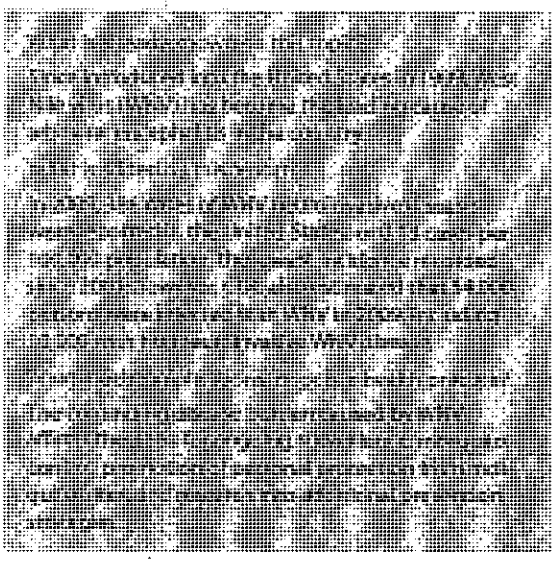
FIGURE 3. Incidence* of cases (N = 386) of West Nile virus neuroinvasive disease,† by age group — ArboNET, United States, 2009



* Per 100,000 population, based on July 1, 2009 U.S. Census estimates.
† Meningitis, encephalitis, or acute flaccid paralysis.

Editorial Note

Since introduced into the United States in 1999, WNV has become the leading cause of arboviral encephalitis in the country. However, in 2009, the reported incidence of WNV neuroinvasive disease in the United States was 0.13 per 100,000 population, the lowest recorded since 2001 (*2*). During



2004–2007, WNV had appeared to reach a stable incidence of approximately 0.4 per 100,000, but incidence dropped to 0.2 per 100,000 in 2008 (*2*) and continued to decline in 2009. This trend might be attributed to variation in populations of vectors and vertebrate hosts, accumulation of immunity in avian amplifying hosts, human behavior (e.g., use of repellents and protective clothing), community-level interventions, reporting practices, or environmental factors (e.g., temperature and rainfall) (*4,5*).

In 2009, evidence of WNV human disease again was detected in all geographic regions of the continental United States. The highest incidence of WNV neuroinvasive disease continued to occur mainly in the west-central United States, likely because of the high efficiency of *Cx. tarsalis* as a WNV vector. Mississippi (31 cases, 1.05 cases per 100,000) continued to be among those states with the highest incidence of WNV neuroinvasive disease. Arizona, which had the second highest incidence of WNV neuroinvasive disease in 2008 (62 cases, 1.0 per 100,000), reported an 81% decrease in cases with 12 cases and an incidence of only 0.18 per 100,000 in 2009 (*1*). After reporting its first two neuroinvasive disease cases in 2008, Washington reported the seventh highest state incidence in 2009 (26 cases, 0.39 per 100,000). These findings illustrate the wide annual variability and focality of WNV transmission.

The findings in this report are subject to at least two limitations. First, ArboNET is a passive surveillance system that depends on clinicians to consider the diagnosis of an arboviral disease, obtain the appropriate diagnostic test, and report any positive results. Diagnosis and reporting likely are incomplete, leading to underestimation of the true incidence of disease. Second, arboviral surveillance programs, testing capacity, and reporting can vary by county, state, or region, affecting incidence estimates.

In the absence of an effective human vaccine, prevention of WNV disease depends on community-level mosquito control and promotion of personal protective measures. Such measures include use of mosquito repellents, barrier protection (e.g., long-sleeved shirts, long pants, and socks), avoiding outdoor exposure, or using personal protection from dusk to dawn. Household measures, such as window screens and covering or draining peridomestic water-holding containers can further decrease the risk for WNV exposure.

Additional information on prevention of WNV infection is available from CDC at http://www.cdc.gov/ncidod/dvbid/westnile/index.htm. An overview of current year WNV transmission activity is available at http://diseasemaps.usgs.gov/wnv_us_human.html.

Acknowledgments

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