別紙

一般的名称	①人血清アルブミン、②人血清アルブミン、③人血清アルブミン*、④人免役グロブリン、⑤乾燥ペプシン処理人免疫グロブリン、⑥乾燥スルホ化人免疫グロブリン、⑦乾燥スルホ化人免疫グロブリン*、⑧乾燥濃縮人活性化プロテインC、⑨乾燥濃縮人血液凝固第Ⅷ因子、⑩乾燥濃縮人血液凝固第Ⅸ因子、⑪乾燥抗破傷風人免疫グロブリン、⑫抗 HBs 人免疫グロブリン、⑬トロンビン、⑭フィブリノゲン加第ⅩⅢ因子、⑮乾燥濃縮人アンチトロンビンⅢ、⑯ヒスタミン加人免疫グロブリン製剤、⑰人血清アルブミン*、⑱人血清アルブミン*、⑲乾燥ペプシン処理人免役グロブリン*、⑳乾燥人血液凝固第Ⅸ因子複合体*、㉑乾燥濃縮人アンチトロンビンⅢ
販売名(企業名)	①献血アルブミン 20 “化血研”、②献血アルブミン 25 “化血研”、③人血清アルブミン “化血研” *、④ “化血研” ガンマーグロブリン、⑤献血静注グロブリン “化血研”、⑥献血ベニロンーⅠ、⑦ベニロン*、⑧注射用アナクトC2,500 単位、⑨コンファクトF、⑩ノバクトM、⑪テタノセーラ、⑫ヘパトセーラ、⑬トロンビン “化血研”、⑭ボルヒール、⑮アンスロビンP、⑯ヒスタグロビン、⑰アルブミン 20%化血研*、⑱アルブミン 5%化血研*、⑲静注グロブリン*、⑳ノバクトF*、㉑アンスロビンP1500 注射用
報告企業の意見	本感染症については、情報入手時点で病原因子は特定されていない。病原因子が細菌類であれば本剤の製造工程中の「無菌ろ過工程」および、細菌よりも小さいウイルスの除去を目的とした平均孔径 19nm 以下の「ウイルス除去膜ろ過工程」により除去されるものと考えられる。また、病原因子がウイルスであれば、「血漿分画製剤のウイルスに対する安全性確保に関するガイドライン（医薬発第 1047 号、平成 11 年 8 月 30 日）」に従ったウイルスプロセスバリデーションの結果から、病原因子は本剤の製造工程において除去・不活化されることが検証されている。以上のように、病原因子が細菌類あるいは既知のウイルスであれば、今回の感染症に対して本剤は一定の安全性を確保していると考える。また、未知のウイルスであっても、既存のウイルス除去・不活化工程の効果が期待される。 現時点で、感染症の流行はインド国内のみで当該生物由来成分の原産国とは離れているため、本剤への直接の影響はなく、緊急の安全対策の必要性もないと考えられるが、感染症は短期間に爆発的に増加することがあるため、今後とも関連情報の収集に努め、本剤の安全性の確保を図っていきたい。

*現在製造を行っていない

Archive Number 20080828.2697
Published Date 28-AUG-2008
Subject PRO/EDR> Undiagnosed fatal illness - India (04): (UP)

UNDIAGNOSED FATAL ILLNESS - INDIA (04): (UTTAR PRADESH)
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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>

[1]
Date: Tue 26 Aug 2008
Source: The Hindustan Times, online [edited]
<http://www.hindustantimes.com/StoryPage/StoryPage.aspx?sectionName=&id=3825990

The mystery virus striking children dead in eastern Uttar Pradesh (UP) has been diagnosed as "acute encephalitis syndrome" by Union Health Ministry experts. Simply put, they do not know what is causing the acute brain fever.

Within weeks, about 800 cases and 150 deaths were reported from 13 districts in UP, and experts predict that the numbers could rise.

"Less than 5 per cent blood and serum samples have tested positive for Japanese encephalitis (JE), which has seen major outbreaks in the region each year," said Dr Shiv Lal, director of the National Institute of Communicable Diseases.

"Usually, at least 15-20 per cent samples test positive for JE during an outbreak, but the low positivity is causing confusion this year [2008]. With 4 crore [40 million] children in 27 districts in UP being vaccinated against JE this year, experts wonder why the fever refuses to go away. There is no problem with the Chinese vaccine SA 14-14-2," said a health ministry official. The virus, approved by World Health Organization, protects against JE. "We suspect some children could have missed the vaccination drive." All the hospitalised children have reported symptoms of acute encephalitis.

"Since less than 5 per cent have tested positive for JE, we are investigating whether the outbreak is a combination of JE and water-borne enterovirus that caused the disease in 2006," said Dr Lal. The Centre is sending a 4-member team comprising a microbiologist, a pediatrician, an entomologist, and an epidemiologist to Lucknow and Gorakhpur to track the outbreak and collect blood and serum samples from hospitalisd children for viral culture.

"Apart from rapid tests for JE done using kits developed by Pune's National Institute of Virology, we will do virus culture to track the elusive cause of the current outbreak," said Dr Lal, adding that the result could be expected within 2 or 3 days of collection of the samples.

[byline: Sanchita Sharma]

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communicated by:
ProMED-mail rapporteur Mary Marshall

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[2]
Date: Wed 27 Aug 2008
From: T Jacob John <vlr_tjjohn@sancharnet.in>

Although the details are skimpy, age distribution and clinical description lacking, yet the available information can be used to propose a provisional diagnosis to be investigated. Heavy rainfall and flooding, febrile illness resembling malaria, and relatively large numbers of death does remind one of leptospirosis. Immediate serological testing for this disease is warranted.

Similar episodes in Orissa and Mumbai a few years ago (all the 3 features above fitted) turned out to be leptospirosis. In Orissa it was for the first time (at least recognized), while in Mumbai the presence of leptospirosis was already known. To add, there is no shortcut to detailed clinical description and elementary epidemiological investigation of cases based on specific diagnostic criteria of the outbreak disease, and exploration of risk factors (to look for transmission pathways). Instead of doing what one can do locally, the complete dependence on experts from elsewhere is not good.

--
Dr T Jacob John
Christian Medical College
Vellore
India
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[Japanese encephalitis virus infection is an unlikely explanation, but still under investigation. - Mod.CP

ProMED-mail thanks Dr John for his comments and looks forward to more information about this outbreak. - Mod.LL]

[see also:
Undiagnosed fatal illness - India (03): (UP) RFI 20080826.2666
Undiagnosed fatal illness - India (02): (UP) RFI 20080811.2478
Undiagnosed fatal illness - India (Uttar Pradesh): RFI 20080331.1194
2007

Japanese encephalitis - India (02) (Uttar Pradesh) 20071026.3486
Undiagnosed viral disease - India (02): (Uttar Pradesh) 20071026.3485
Undiagnosed viral disease - India: (Uttar Pradesh) 20071022.3440
Japanese encephalitis - India (Uttar Pradesh) 20070930.3233
2006

Japanese encephalitis - India (Uttar Pradesh) (03): vaccine safety 20061222.3583
Leptospirosis - India (Gujarat): not hantavirus 20060831.2476
Leptospirosis - India (Maharashtra) 20060726.2058
Leptospirosis - India (Kerala) 20060609.1612
Leptospirosis - India (Karnataka) 20060123.0226
2005

Undiagnosed deaths - India (Uttar Pradesh) (02) 20051115.3342
Undiagnosed deaths - India (Uttar Pradesh): RFI 20051113.3322
Leptospirosis - India (Maharashtra) 20050811.2348
2004

Leptospirosis - India (South Gujarat) (02) 20040908.2509
Leptospirosis - India (South Gujarat) 20040902.2441
Leptospirosis - India (Tamil Nadu) 20040226.0602]

.....cp/ll/msp/sh

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別紙様式第2-1

No. 18

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. 7. 11	該当なし	

一般的名称	(製造販売承認書に記載なし)	研究報告の公表状況		公表国
販売名(企業名)	合成血-LR「日赤」(日本赤十字社) 照射合成血-LR「日赤」(日本赤十字社)		Komar N, Clark GG. Rev Panam Salud Publica. 2006 Feb;19(2):112-7.	米国

研究報告の概要

○ラテンアメリカおよびカリブ諸国のウエストナイルウイルスの活動性

目的:ウエストナイルウイルス(WNV)は、2001年に初めてカリブ海地域で検出されて以来、当地で急速に広がった。アメリカ大陸熱帯地域におけるWNV伝播の最近の知見について要約する。

方法:発表された文献のレビューを行い、主要な公衆衛生担当者に意見を求め、未発表データを入手した。

結果:WNV感染症は、ヒトでは2001年に初めてケイマン諸島およびフロリダキーの住民に発症し、2002年早期にジャマイカの健常な鳥類検体に初めて認められた。2002年のWNV感染症の血清学所見は、グアドループ、ドミニカ共和国と東部メキシコでウマ、ニワトリおよび野生鳥類に検出された。2003年には、WNVはメキシコおよび中央アメリカ北部で蔓延し、血清学的エビデンスはバハマ、プエルトリコとキューバで検出された。2004年9月～10月には、コロンビアとトリニダードで南米生態系におけるWNV活動の最初の血清学的エビデンスが表面化し、当地では家畜のWNV中和抗体保有率が高かった。

結論:ラテンアメリカおよびカリブ海地域において、ウマ、ヒトおよびトリでの疾患報告が少ないことは不可解である。熱帯生態系での疾患の低減について、ウイルスの減弱化あるいは他の可能性を検討するため、分離株が必要である。

報告企業の意見	今後の対応
ラテンアメリカおよびカリブ海地域の動物や鳥類において、ウエストナイルウイルスの抗体陽性率は高くなっているが疾患報告は少ない。この不可解な熱帯生態系での疾患の低減について、原因を検討するため分離株が必要であるとの報告である。	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発生に備え、緊急対応の準備を進めている。今後も引き続き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-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

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Informe especial / Special report

West Nile virus activity in Latin America and the Caribbean

Nicholas Komar[1] *and Gary G. Clark*[2]

Suggested citation Komar N, Clark GG. West Nile Virus activity in Latin America and the Caribbean. Rev Panam Salud Publica. 2006;19(2):112–7.

ABSTRACT **Objectives.** *West Nile virus* (Flavivirus: Flaviviridae; *WNV) has spread rapidly throughout the Caribbean Basin since its initial detection there in 2001. This report summarizes our current knowledge of WNV transmission in tropical America.*
Methods. *We reviewed the published literature and consulted with key public health officials to obtain unpublished data.*
Results. *West Nile virus infections first appeared in human residents of the Cayman Islands and the Florida Keys in 2001, and in apparently healthy Jamaican birds sampled early in 2002. Serologic evidence of WNV infection in 2002 was detected in horses, chickens and resident free-ranging birds in Guadeloupe, the Dominican Republic, and eastern Mexico. In 2003, WNV spread in Mexico and northern Central America, and serologic evidence was detected in the Bahamas, Puerto Rico and Cuba. In 2004, the first serologic evidence of WNV activity in South American ecosystems surfaced in September-October in Colombia and Trinidad, where domestic animals circulated WNV-neutralizing antibodies.*
Conclusions. *The sparse reports of equine, human and avian disease in Latin America and the Caribbean is puzzling. Isolates are needed to evaluate viral attenuation or other possible explanations for reduced disease burden in tropical ecosystems.*

Key words West Nile virus; Latin America; Caribbean region; arboviruses; population surveillance; flavivirus.

INTRODUCTION

Since West Nile virus (*Flavivirus: Flaviviridae;* WNV) first appeared in the Western Hemisphere in New York in 1999, it has spread rapidly across the North American continent, causing large numbers of human cases with neurologic disease and death, and even greater amounts of milder disease characterized principally by fever and rash. Horses and hundreds of species of birds also fell victim to this emerging virus (1). West Nile virus spread southward into the Caribbean Basin and Latin America as well, where its public health impact remains poorly understood and surveillance systems are unprepared to track its spread. The virus was first detected in 2001, in Jamaica and the Cayman Islands. In 2005 WNV activity was reported from many locations in the Caribbean Basin, Mexico, Central America and the northern rim of South America (Figure 1). In order to package our current knowledge of WNV activity and surveillance results from various locations within tropical America, we reviewed published reports and some unpublished data available from public health officials, and provide a summary below. We also comment on the significance of the surveillance findings and on the potential public health threat of WNV in tropical America.

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[2] Centers for Disease Control and Prevention, Division of Vector-Borne Infectious Diseases, 1324 Calle Cañada, San Juan 00920, Puerto Rico.

METHODS

We reviewed peer-reviewed publications and government reports and consulted with key public health officials within Caribbean Basin countries to obtain unpublished data.

RESULTS

West Nile virus detected in 2001

In the State of Florida (United States of America), Blackmore et al. described surveillance findings for WNV in two epidemic foci in 2001—a northern focus and a southern focus (2). The northern focus was characterized by humid temperate forests typical of the southeastern United States but unlike tropical ecosystems in Latin America. The first evidence for WNV activity here was a dead American Crow (*Corvus brachyrhynchos*) in June, 2001. Nine human cases of West Nile neurologic disease (WNND) were reported between July and October. Entomologic investigations near case residences in July detected WNV in three species of *Culex* (*Culex*) mosquitoes: *Culex quinquefasciatus*, *C. nigripalpus* and *C. salinarius* (3, 4). The first two of these species are common further south in the Caribbean Basin.

The southern epidemic focus in Florida was more typical of Caribbean Island ecology and occurred in the Florida Keys. A human case of WNND with onset in July, 2001, represented the earliest indication of WNV activity there. Two more human cases were reported with onsets in August and September. West Nile virus was isolated from dead corvids (e.g., Fish Crow, *Corvus ossifragus*) and *Streptopelia* doves (probably *Streptopelia decaocto*, Eurasian Collared-Dove, an introduced species that is also abundant in the Bahamas). Entomologic investigations were carried out throughout the Keys during the last quarter of 2001 (5). Infection rates were highest in *Anopheles atropos* (3 of 410), *Deinocerites cancer* (2 of 845) and *Ochlerotatus taeniorhynchus* (2 of 9288). This last species is a ferocious human biter, and abundant in coastal locations throughout the Caribbean Basin. About 20 000 other mosquitoes tested negative.

Follow-up mosquito surveillance studies in the Florida Keys in the following two years yielded no WNV in more than 30 000 mosquitoes tested in 2002, but the virus was detected in 10 pools representing 53 673 mosquitoes in 2003 (6). In 2003, infections were detected from May–September. Infected species included *C. quinquefasciatus* (minimum infection rate 1.7 per 1 000), *C. nigripalpus* (0.9), *O. taeniorhynchus* (0.9), *O. condolescens* (0.6) and *C. erraticus* or *declarator* (0.6). No infections were detected in either *A. atropos* or *D. cancer* even though more than 5 000 of each species were tested. These findings suggest that either WNV became endemic in the Florida Keys but dropped below levels of detection in 2002, or that multiple, temporally dispersed introductions occurred, resulting in transmission activity in both 2001 and 2003.

Although the circumstances of WNV introduction into the Florida Keys are unknown, the likely explanation is that migrating birds served as dispersal hosts, seeding the virus into potential transmission foci during their southward migration in the fall of 2000. By late 2000, WNV activity was reported as far south as North Carolina in the continental United States (7). The virus had probably spread even further south at undetectable levels, to be amplified by resident birds and *Culex* mosquitoes during the warmer spring and early summer months of 2001. While migrating birds are a convenient explanation of WNV dispersal, other possible means of dispersion exist, such as infected mosquitoes that are accidentally transported via surface transportation or airplanes.

South of the Florida Keys, a human WNND case with no history of international travel was reported with onset on August 2, 2001, from tiny Cayman Brac (area 14 square miles [36 square kilometers], population 1 200), in the Cayman Islands, south of Cuba (8). Assuming an incubation period of 2–15 days in people, this infection probably occurred in late July, about the same time that the first human case was infected in the Florida Keys. However, the laboratory diagnosis of this case was not announced until October 15, 2001. Laboratory tests were positive for anti-WNV IgM (indicating recent infection) and a 90% plaque-reduction neutralizing antibody titer ($PRNT_{90}$) of 1:1280, compared with a $PRNT_{90}$ of 1:80 and <1:10 for St. Louis encephalitis virus (SLEV) and Dengue-2 virus, respectively (CDC, unpublished data).

More data supporting WNV transmission activity in the Caribbean Basin in 2001 came from Jamaica, where a Smithsonian Institution-New York State Health Department research team reported 17 seropositive resident birds of 348 collected in 3 of 4 study sites, all on the western side of the island (9). The samples were collected in the first three months of 2002 but probably reflected transmission that had occurred months earlier in 2001. Seropositive bird species included *Turdus aurantius* (n = 4), *Myiopagis cotta* (2), *Coereba flaveola* (2), *Tiaris bicolor* (2), and one each of seven other species. Seropositivity was determined by comparing $PRNT_{90}$ titers for WNV, SLEV and Ilheus virus, a South American flavivirus that is genetically closely related to SLEV, but not in the same antigenic complex as SLEV and WNV (10). All 17 WNV-positive samples were at least four-fold greater in WNV titer than other flavivirus titers. Three samples were positive for SLEV-neutralizing antibodies, which has been previously isolated in Jamaica (11). No samples were positive for Ilheus virus, but five additional samples had similar titers for both SLEV and WNV, and these were classified as undetermined flavivirus infections. The 2001 WNV activity in Jamaica and the Cayman Islands was most likely the result of the same introduction mechanism as postulated for extreme southern Florida: southward dispersal of the virus below limits of detection via migrating birds late in 2000.

Operating under the premise that birds would carry WNV along migration routes, efforts were initiated to detect WNV activity on the southern side