random start point and random direction for sampling.

At each participating household, all residents present and aged ≥5 years were asked to provide a blood sample and demographic information. Serum samples were tested for IgM and IgG antibodies to dengue virus by ELISA. The seroincidence of recent dengue infection was defined by IgM antibodies ≥0.2 optical density (OD). Seroprevalence was defined as the presence of IgG antibodies ≥1:40. Data were weighted to reflect probability of selection, taking into account the population and numbers of households per census tract and size of household.

In Matamoros, 240 households were visited during December 5--10, and 143 (59.6%) had residents at home. Blood samples were obtained from 131 persons in 111 homes. Of these samples, 30 were anti-dengue IgM positive (weighted prevalence: 22.8%; 95% confidence interval [CI] = 13.3%--32.3%), and 101 were IgG positive (weighted prevalence: 76.6%; CI = 64.7%--88.5%). In Brownsville, 346 households were visited during December 12--15, and 161 (46.5%) had residents at home. Blood samples were obtained from 141 persons in 118 homes. Of these samples, four were anti-dengue IgM positive (weighted prevalence: 2.5%; CI = 0%--5.4%) and 47 were IgG positive (weighted prevalence: 38.2%; CI = 26.7%--49.8%). Of 24 Brownsville participants with no history of travel outside the United States, six (25%) were seropositive for IgM or IgG antibodies to dengue.

Reported by: *A Abell, PhD, B Smith, MD, M Fournier, MD, Texas Dept of State Health Svcs, Harlingen, Texas; T Betz, MD, L Gaul, PhD, Texas Dept of State Health Svcs, Austin, Texas; JL Robles-Lopez, MD, CA Carrillo, MD, Jurisdicción Sanitaria No. III de Matamoros, Matamoros, Tamaulipas; A Rodríguez-Trujillo, MD, Servicios de Salud de Tamaulipas, Cd. Victoria, Tamaulipas; C Moya-Rabelly, MD, Mexico Section of the US-Mexico Border Health Commission, Tijuana, Baja California; O Velasquez-Monroy, MD, C Alvarez-Lucas, MD, Centro Nacional de Vigilancia Epidemiológica y Control de Enfermedades, Mexico, DF; P Kuri-Morales, MD, L Anaya-Lopez, MD, Dirección General de Epidemiología, México, DF. M Hayden, PhD, National Center for Atmospheric Research, Boulder, Colorado. E Zielinski-Gutierrez, DrPH, J Muñoz, PhD, M Beatty, MD, I Sosa, Div of Vector-Borne Infectious Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases; S Wenzel, MPH, Career Development Div, Office of Workforce and Career Development; M Escobedo, MD, S Waterman, MD, Div of Global Migration and Quarantine, National Center for Preparedness, Detection, and Control of Infectious Diseases; M Ramos, MD, BK Kapella, MD, H Mohammed, PhD, R Taylor, PhD, J Brunkard, PhD, EIS officers.*

Editorial Note:

DHF incidence has increased in the Western Hemisphere in Latin America and the Caribbean during the past two decades (*3*). Over this period, the epidemiology of dengue in Mexico and Texas has changed. Since 1995, when all four dengue serotypes were identified as circulating in Mexico, an increasing percentage of reported dengue cases in Mexico have been DHF (*7*). In the Mexican border state of Tamaulipas, all four serotypes were first reported in circulation in 1995, and the proportion of reported DHF cases increased from 2.2% in 2000 to 23.4% in 2006. In south Texas, all dengue serotypes have circulated periodically (*3,8*), but locally acquired DHF has been reported only recently (*9*). The first report of locally acquired DHF in Texas, published in 2004, described a fatal case involving a woman originally from Southeast Asia (*9*). She presumably had acquired her first dengue infection in Asia and her second dengue infection in Val Verde, Texas, near the U.S.-Mexico border. However, the DHF case described in this report is the first in a Texas resident who was native to the U.S.-Mexico border area. Case-finding activities during the dengue outbreak identified 15 additional DHF cases on the Texas side of the border.

Entomologic, serologic and virologic conditions are now such that locally acquired DHF can occur in south Texas. The principal dengue vector, the *Aedes aegypti* mosquito, is well established in south Texas, as is *Aedes albopictus*, which also is capable of transmitting dengue

(*7,10*; TDSHS, unpublished data, 2007). The finding that 38% of surveyed Brownsville residents have IgG antibodies to dengue indicates that a substantial proportion of the city population has been infected with the dengue virus and might be more susceptible to DHF if they receive a second infection with a heterologous dengue serotype. The presence in Brownsville of multiple dengue serotypes since 1980 might increase the likelihood for secondary dengue infections from a different serotype and increase the risk for DHF.

The findings in this report are subject to at least two limitations. First, more comprehensive laboratory testing on the U.S. side of the border during the 2005 outbreak likely accounted for the greater percentage of patients meeting DHF criteria among hospitalized dengue patients in Cameron County compared with Matamoros. As such, the results for these two sites are not directly comparable. Second, because anti-dengue IgM antibodies do not always remain elevated 2--3 months after infection, especially after a second infection, the serosurvey conducted during December 5--15 likely underestimated the number of recent dengue infections in Brownsville and Matamoros.

Health authorities along the Texas-Tamaulipas border should consider strengthening surveillance for dengue fever, given the potential for future outbreaks with increased risk for DHF. Maintaining active virologic surveillance for circulating serotypes also is important to provide early warning of possible epidemics. Clinicians in the south Texas area and members of the public should be aware of the potential for DHF in addition to dengue fever in the region. Furthermore, clinicians should be trained to recognize and manage DHF. Early recognition and diagnosis of DHF and careful fluid management can reduce the case fatality rate in cases with shock to less than 1%. Public health officials should continue outreach activities to advise communities of prevention measures, including effective mosquito surveillance and reduction programs.

Acknowledgments

This report is based, in part, on contributions from DJ Gubler, Asia-Pacific Institute of Tropical Medicine and Infectious Diseases, Honolulu, Hawaii; J Ramirez, City of Brownsville Public Health Dept, Texas; R Burton, Texas Dept of State Health Svcs; and state and local health departments in Texas and Tamaulipas, Mexico.

References

1. Rothman AL. Immunology and immunopathogensis of dengue infection. Adv Virus Res 2003;60:397--419.
2. World Health Organization. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd ed. Geneva, Switzerland: World Health Organization, 1997. Available at http://www.who.int/csr/resources/publications/dengue/Denguepublication/en.
3. Gubler DJ. Dengue and dengue hemorrhagic fever. In: Guerrant R, Walker D, Weller P, eds. Tropical infectious diseases. 2nd ed. Philadelphia, PA: Elsevier; 2006:813--22.
4. Leitmeyer KC, Vaughn DW, Watts DM, et al. Dengue virus structural differences that correlate with pathogenesis. J Virol 1999;73:4738--47.
5. Rico-Hesse R. Dengue virus evolution and virulence models. Clin Infect Dis 2007;44:11462--6.
6. Turner AG, Magnani RJ, Shuaib M. A not quite as quick but much cleaner alternative to the expanded programme on immunization (EPI) cluster survey design. Int J Epidemiol 1996;25:198--203.
7. Diaz FJ, Black WC, Farfan-Ale JA, Loroño-Pino MA, Olson KE, Beaty BJ. Dengue virus circulation and evolution in Mexico: a phylogenic perspective. Arch Med Res 2006;37:760--73.
8. CDC. Dengue fever at the US-Mexico border, 1995--1996. MMWR 1996;45:841--4.
9. Setlik RF, Ouellette D, Morgan J, et al. Pulmonary hemorrhage syndrome associated with an autochthonous case of dengue hemorrhagic fever. South Med J 2004;97:688--91.

10. Hayes JM, Rigau-Perez JG, Reiter P, et al. Risk factors for infection during a dengue-1 outbreak in Maui, Hawaii, 2001. Trans R Soc Trop Med Hyg 2006;100:559--66.

* ≤100,000 platelets/mm^3.

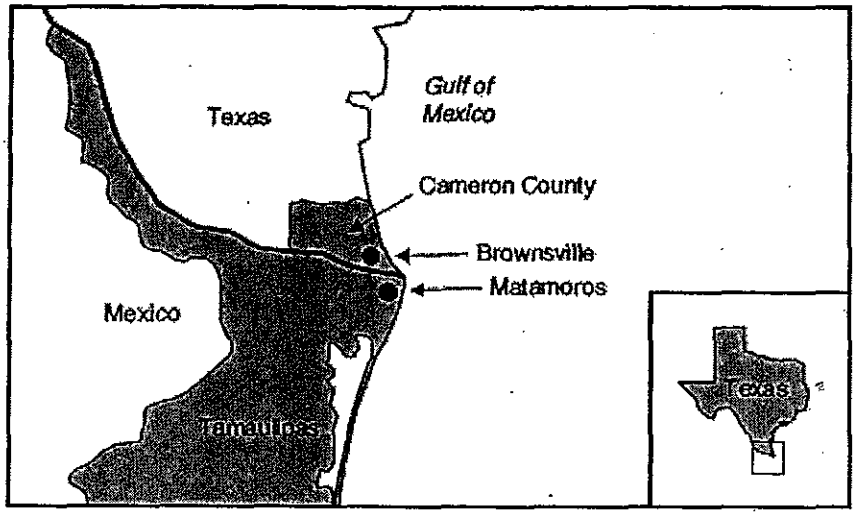
† Boletín Epidemiolgía [Spanish] México, D.F. Dirección General de Epidemiología, 2000--2006. Available at http://www.dgepi.salud.gob.mx/boletin/boletin.htm.

§ Defined as the presence of anti-dengue IgM antibody, dengue viral identification by polymerase chain reaction, or virus isolation from a blood sample of a patient with clinically compatible symptoms.

¶ DHF is classified into four grades of severity; grades III and IV are considered to be dengue shock syndrome. Grade I: Fever accompanied by nonspecific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test and/or easy bruising. Grade II: Spontaneous bleeding in addition to the manifestations of Grade I patients, usually in the forms of skin or other hemorrhages. Grade III: Circulatory failure manifested by a rapid, weak pulse and narrowing of pulse pressure or hypotension, with the presence of cold, clammy skin and restlessness. Grade IV: Profound shock with undetectable blood pressure or pulse (*2*).

Figure 1

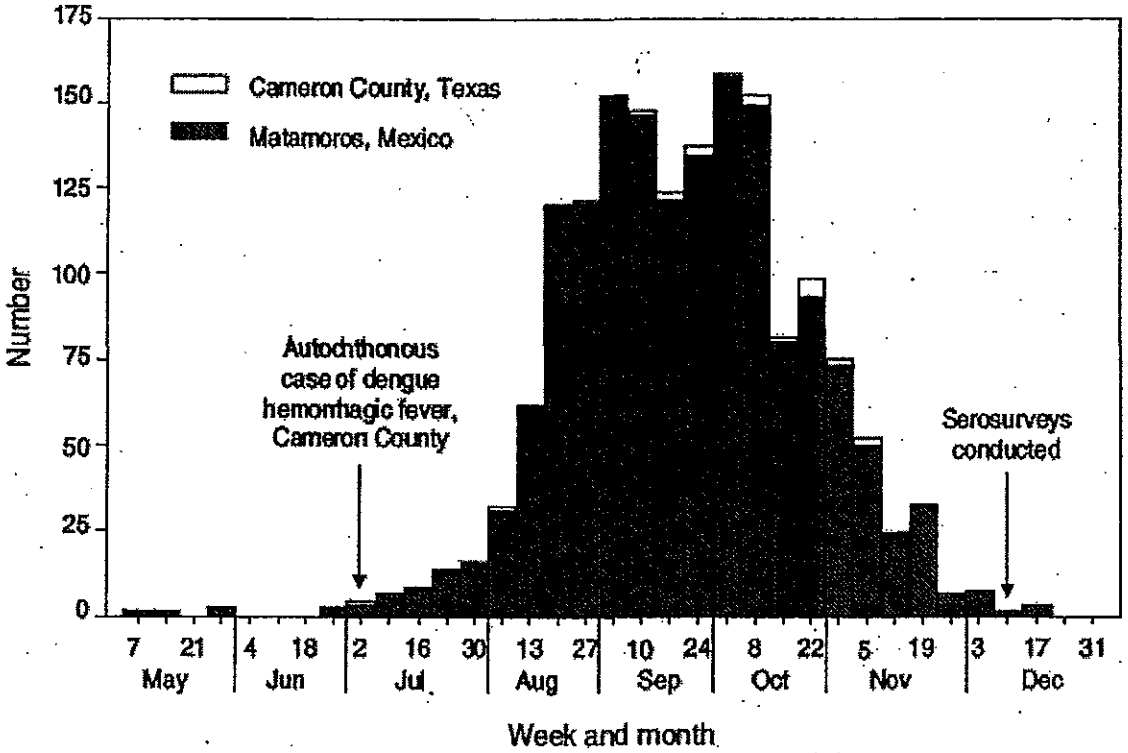
FIGURE 1. Jurisdictions affected by dengue fever outbreak — Texas–Mexico border, 2005



Return to top.

Figure 2

FIGURE 2. Number of cases of dengue fever, by week of report — City of Matamoros, Mexico,* and Cameron County, Texas,† 2005



*n = 1,596.
†n = 25.

Return to top.

Box

BOX. World Health Organization case definition for dengue hemorrhagic fever

The following must all be present:

- Fever, or history of acute fever, lasting 2–7 days, occasionally biphasic.
- Hemorrhagic tendencies, evidenced by at least one of the following:
  - — a positive tourniquet test;
  - — petechiae, ecchymoses, or purpura;
  - — bleeding from the mucosa, gastrointestinal tract, injection sites, or other locations;
  - — hematemesis or melena.
- Thrombocytopenia ($\leq$100,000 platelets/mm^3).
- Evidence of plasma leakage because of increased vascular permeability, manifested by at least one of the following:
  - — an increase in the hematocrit $\geq$20% above average for age, sex, and population;
  - — a decrease in the hematocrit following volume-replacement treatment $\geq$20% of baseline;
  - — signs of plasma leakage such as pleural effusion, ascites, and hypoproteinemia.

SOURCE: World Health Organization. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd ed. Geneva, Switzerland: World Health Organization, 1997. Available at http://www.who.int/csr/resources/publications/dengue/Denguepublication/en.

Return to top.

SAFER·HEALTHIER·PEOPLE™
Morbidity and Mortality Weekly Report
Centers for Disease Control and Prevention
1600 Clifton Rd, MailStop E-90, Atlanta, GA
30333, U.S.A

別紙様式第2-1
番号15

医薬品
医薬部外品　　研究報告　調査報告書
化粧品

識別番号・報告回数			報告日	第一報入手日 2007年6月11日	新医薬品等の区分	厚生労働省処理欄
一般的名称	①②ポリエチレングリコール処理人免疫グロブリン ③人免疫グロブリン	研究報告の公表状況	Transactions of the Royal Society of Tropical Medicine and Hygiene 2007; 101(7): 738-739	公表国 日本		
販売名 （企業名）	①献血ヴェノグロブリン-IH ヨシトミ（ベネシス） ②ヴェノグロブリン-IH（ベネシス） ③グロブリン-Wf（ベネシス）					

研究報告の概要

28歳の日本人女性が、2006年6月29日から2006年7月4日までベトナムを、2006年7月4日から10日まで中国を訪問した。7月6日に、彼女は関節痛を伴う高熱を呈した。6日後に、四肢に斑点状丘疹を生じた。彼女は、7月11日に我々のクリニックを訪問した。発熱または出血の徴候が観察されなかったにもかかわらず、臨床検査では血小板減少症（39000個/μL）と白血球減少症（1730の白血球数/μL）を示した。デングウイルス・ゲノムは、7、14または21日目に、血漿または末梢血単核細胞（PBMC）サンプル中には検出されなかった。しかしながら、デングウイルス-1型（DENV-1）ゲノムが、7、8及び14日目の尿サンプル、並びに7日目のだ液サンプルから検出された。尿サンプルからのPCR産物のヌクレオチド配列の分析から、検出されたゲノムはデングウイルス-1のゲノムであることが確認された。
DENV感染は、通常血清または血漿サンプルでELISAによるデング特異的IgM及びRT-PCRによるウイルスゲノムの検出によって確認される。RT-PCR試験は疾患の初期段階のみ検出可能であり、ELISA試験は疾患の初期は陰性であって予想的診断を下すことができるに過ぎない。従って、検査法の組合せが、デングウイルス感染症の確度の高い診断を下すために必要である。尿とだ液サンプルは侵襲的方法を使用せずに集めるのが容易であり、尿はかなりの量を集めることができる。更なる検討が必要であるが、本研究の結果から、尿と唾液のDENVゲノムの検出が、ウイルス性出血の小児にとって有効且つ支援となる代替診断法となり得ることを示唆している。

報告企業の意見	今後の対応
デング熱患者の血漿中ではなく尿及び唾液中からデングウイルスが検出されたとの報告である。 血漿分画製剤からのデングウイルス伝播の事例は報告されていない。万一、原料血漿にデングウイルスが混入しても、BVD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、本剤の製造工程において十分に不活化・除去されると考えている。	本報告は本剤の安全性に影響を与えないと考えるので、特段の措置はとらない。

使用上の注意記載状況・その他参考事項等

代表として献血ヴェノグロブリン-IH ヨシトミの記載を示す。
2. 重要な基本的注意
(1) 本剤の原材料となる献血者の血液については、HBs抗原、抗HCV抗体、抗HIV-1抗体、抗HIV-2抗体、抗HTLV-I抗体陰性で、かつALT（GPT）値でスクリーニングを実施している。更に、プールした試験血漿については、HIV-1、HBV及びHCVについて核酸増幅検査（NAT）を実施し、適合した血漿を本剤の製造に使用しているが、当該NATの検出限界以下のウイルスが混入している可能性が常に存在する。本剤は、以上の検査に適合した血漿を原料として、Cohnの低温エタノール分画で得た画分からポリエチレングリコール4000処理、DEAEセファデックス処理等により人免疫グロブリンを濃縮・精製した製剤であり、ウイルス不活化・除去を目的として、製造工程において60℃、10時間の液状加熱処理及び濾過膜処理（ナノフィルトレーション）及びpH3.9～4.4の条件下での液状インキュベーション処理を施しているが、投与に際しては、次の点に十分注意すること。

153

Transactions of the Royal Society of Tropical Medicine and Hygiene (2007) 101, 738–739

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevierhealth.com/journals/trst

CASE REPORT

Confirmation of dengue virus infection by detection of dengue virus type 1 genome in urine and saliva but not in plasma

Y. Mizuno[a,*], A. Kotaki[b], F. Harada[b], S. Tajima[b], I. Kurane[b], T. Takasaki[b]

[a] *Disease Control and Prevention Centre, International Medical Centre of Japan, 1-21-1, Toyama, Shinjuku, Tokyo 162-8655, Japan*
[b] *Department of Virology 1, National Institute of Infectious Diseases, Tokyo, Japan*

Received 7 November 2006; received in revised form 5 February 2007; accepted 5 February 2007
Available online 5 April 2007

KEYWORDS
Dengue fever;
Dengue hemorrhagic fever;
Diagnosis;
PCR;
Urine;
Saliva

Summary We successfully detected dengue virus (DENV) genome in urine and saliva but not in plasma samples from a Japanese dengue fever patient. The results of the present study suggest that detection of DENV genome in urine and saliva can be an effective diagnostic method, particularly for children with viral hemorrhage.

1. Case report

A 28-year-old Japanese woman visited Vietnam from June 29 to July 4 2006 and China from 4 to 10 July 2006. On 6 July, she developed a high fever with arthralgia. Six days later, maculopapular rashes appeared on her limbs. She visited our clinic (International Medical Centre of Japan) on 11 July. Although no fever or sign of hemorrhage was observed, laboratory tests showed thrombocytopenia (39 000 platelets/μl) and leukopenia (1730 white blood cells/μl). A diagnosis of dengue fever was considered, and RT-PCR, IgM-capture ELISA and IgG ELISA were carried out (Nawa et al., 2001).

Anti-dengue virus (DENV) IgM and IgG were identified in plasma samples on days 7, 14 and 25 after the onset of symptoms (Table 1). These samples were examined for virus genome by real-time RT-PCR (TaqMan RT-PCR) (Ito et al., 2004). DENV genome was not detected in plasma or peripheral blood mononuclear cells (PBMC) samples on day 7, 14 or 21. However, DENV-type 1 (DENV-1) genome was detected in urine samples on days 7, 8 and 14, and in a saliva sample on day 7.

Nucleotide sequences of PCR products from urine samples were determined with BigDye Terminator version 3.1 (Applied Biosystems, Foster City, CA, USA) and PCR primers. Sequence analysis with a PRISM 3100 Avant Genetic Analyzer (Applied Biosystems) confirmed that the detected genome

* Corresponding author. Tel.: +81 3 3202 7181; fax: +81 3 3202 1012.
E-mail addresses: yamizuno@imcj.hosp.go.jp, mizunomd@hotmail.com (Y. Mizuno).

0035-9203/$ – see front matter © 2007 Royal Society of Tropical Medicine and Hygiene. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.trstmh.2007.02.007

Rohwer, Robert presentation at the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) Feb 12, 2004. Recent experimental studies in animals regarding TSE infectivity in blood and transfusion transmission of TSE's - Review of recent experiments in rodents and in sheep.

Taylor DM, Fernie K, Reichl HE, Somerville RA. 2000. Infectivity in the blood of mice with a BSE-derived agent. J Hosp Infect 46(1):78-79.

Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC), October 31, 2005. Presentations by FDA staff and discussions by TSEAC on FDA's Risk Assessment for Potential Exposure to Variant Creutzfeldt-Jakob Disease in Human Plasma-Derived Antihemophilic Factor (FVIII) Products.

United Kingdom National CJD Surveillance Unit - Edinburgh, Scotland, 2006. [http://www.cjd.ed.ac.UK/figures.htm] - Results as of March 31, 2006.

United Kingdom National CJD Surveillance Unit - Edinburgh, Scotland, 2006. [http://www.cjd.ed.ac.UK/figures.htm - results as of Aug 4, 2006; accessed on August 14, 2006)

United Kingdom Office for National Statistics. Ninety Population Trends. Winter, 1997. [http://www.statistics.gov.UK/downloads/theme_population/PT90book_V2.pdf - Accessed on June 14, 2006]

Wadsworth JD, Joiner S, Hill AF, Campbell TA, Desbruslais M, Luthert PJ, Collinge J. 2001. Tissue distribution of protease resistant prion protein in variant Creutzfeldt-Jakob disease using a highly sensitive immunoblotting assay. Lancet; 358:171-80.

Will RG, Ironside JW, Zeidler M, Cousens SN, Estibeiro K, Alperovitch A, Poser S, Pocchiari M, Hofman A, Smith PG. (1996) A new variant of Creutzfeldt-Jakob disease in the UK. Lancet. 347(9006):921-5.

World Health Organization. WHO Guidelines on Tissue Infectivity in Transmissible Spongiform Encephalopathies. In: Asher D, Padilla A, editors.; 2005; Geneva: WHO; 2005, 172 pages (accessed August 2006 at http://wdfww.who.int/bloodproducts/TSE/WHO%20TSE%20Guidelines%20FINAL-22%20JuneupdatedNL.pdf)

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
				2007. 9. 25	該当なし	

一般的名称	解凍人赤血球濃厚液	研究報告の公表状況		公表国
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)		ABC Newsletter. 2007 Sep 14.	米国

研究報告の概要

○感染症最新情報:シャーガス病
AABBは米国疾病対策予防センター(CDC)からAABBシャーガス病バイオビジランス・ネットワークを強化するための資金提供を受けた。AABBによると、「これによって、参加している検査施設と行政双方にとって、利便性とシステムの価値が高まるだろう」とのことである。このネットワーク(電子的疾病サーベイランス報告システム)は、シャーガス病の病原因子である*Trypanosoma cruzi*抗体陽性の供血者のスクリーニングと確認検査を検知する。このプログラムのウェブサイトによると、2007年9月13日時点で710件の供血が繰り返し*T. cruzi*抗体陽性となり、追加のRIPA検査(放射性免疫沈降法)を実施した。このうち196検体がRIPA陽性、486検体が陰性だった。残りの検体については結果保留となっている。13の検査施設がシャーガス・ネットワークにデータを報告した。18施設が報告のために現在アクセスしている。

報告企業の意見	今後の対応
AABBシャーガス病バイオビジランス・ネットワークによると、2007年9月13日時点で710件の供血が繰り返し*T. cruzi*抗体陽性となり、追加のRIPA検査では196検体が陽性、486検体が陰性だったとの報告である。	日本赤十字社は、輸血感染症対策として献血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、シャーガス病の既往がある場合には献血不適としている。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

解凍赤血球濃厚液「日赤」
照射解凍赤血球濃厚液「日赤」
解凍赤血球-LR「日赤」
照射解凍赤血球-LR「日赤」

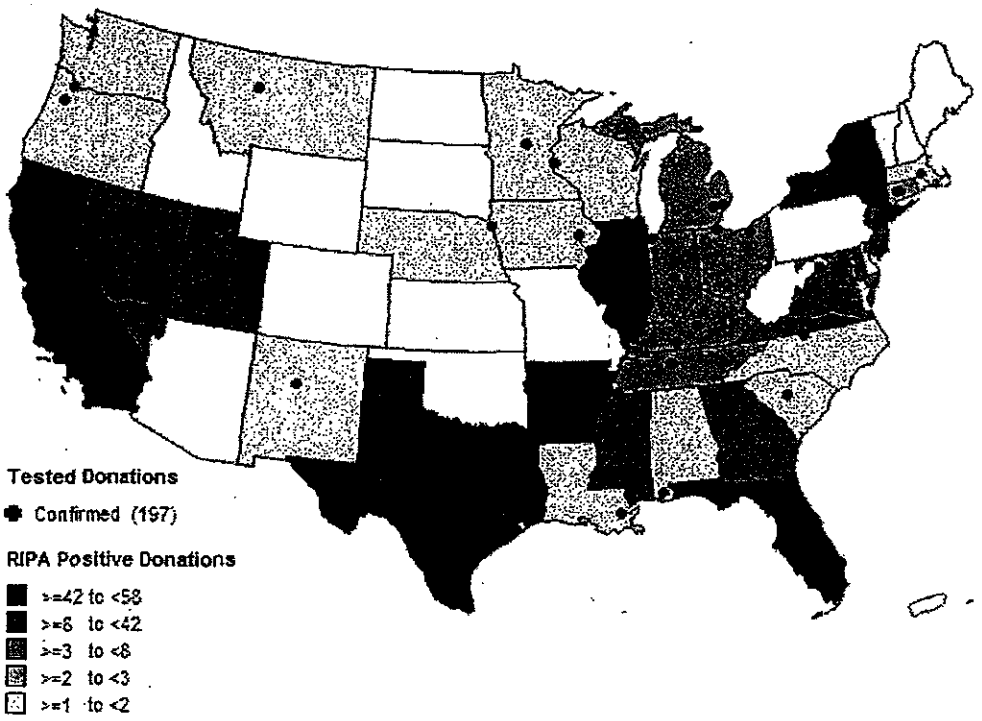
血液を介するウイルス、
細菌、原虫等の感染
vCJD等の伝播のリスク

24

INFECTIOUS DISEASE UPDATES (continued from page 18)

CHAGAS' DISEASE

AABB has received funding from the Centers for Disease Control and Prevention to explore enhancements to the AABB Chagas' Disease Biovigilance Network. According to AABB, "the enhancements would improve usability and value of the system for both participating laboratories and the public." The network – a custom electronic disease surveillance reporting system – tracks screening and confirmatory testing of blood donors with antibodies to *Trypanosoma cruzi*, the agent of Chagas' disease. Source: *AABB Weekly Report*, 9/7/07. According to the program's Web site, as of September 13, 710 repeat reactive donations were tested by the supplemental RIPA test for the antibody to *T. cruzi*, the agent for Chagas' disease. 196 of the repeat reactive donations were RIPA positive; 486 were RIPA non-reactive. Results are pending on the remaining samples. Thirteen testing laboratories reported data into the Chagas Network; eighteen testing laboratories now access the Chagas Network for reporting purposes.



Source: www.aabb.org/Content/Programs_and_Services/Data_Center/Chagas/chagas.htm

INFLUENZA, AVIAN

German health authorities last week ordered the slaughter of more than 200,000 ducks at two farms in Bavaria after tests indicated the presence of the H5N1 strain of bird flu. The head of Bavaria's state office for health and food safety, Volker Hingst, called the slaughter "a purely precautionary measure," taken after "laboratory indications of H5N1" were found. The birds showed no overt signs of the disease, he said. The two farms are located near Schwandorf, east of Nuremberg. Last month, more than 160,000 ducks were slaughtered at another Bavarian poultry farm following an outbreak of the disease. Officials have said that contaminated straw was the likely source in that case. The two new farms with infected ducks are subsidiaries of that farm, authorities said. (Source: Associated Press, 9/7/07) ♦