## Finnish Parliament Finds Red Cross MSM Policy Justified

The Finnish Red Cross Blood Service policy imposing a lifetime ban on blood donation on men who have had sex with men cannot be considered unlawful, Finland's parliamentary ombudsman said in a statement Monday (6/30/08).

The ombudsman, Riitta-Leena Paunio, said in the statement that the decision was based on "appropriately reasoned epidemiological information to the effect that sex between men clearly increases the risk of contracting serious blood-transmitted diseases, such as HIV and hepatitis B and C, and thereby increases the safety risk in blood transfusion.... The ombudsman emphasizes that the ban is not due to sexual orientation, which enjoys constitutional protection against discrimination, but rather to sexual behavior."

The ombudsman pointed out that in addition to gay men, the Finnish Red Cross does not accept blood from anyone over 65 years of age or people who had visited Britain during the bovine spongiform encephalopathy outbreak. The ombudsman was responding to two complaints that alleged the Blood Service was violating the constitutional prohibition of discrimination in considering sex between men to be a permanent obstacle to blood donation.

According to the ombudsman's opinion, the measures undertaken by the Blood Service are not discriminatory and, hence, not in contravention of the Constitution. "The ombudsman considers that there is appropriate justification for regarding sex between men as a permanent obstacle to blood donation. ...At present, sex between men still carries an elevated risk of HIV infection. Statistics from the National Public Health Institute of Finland indicate that 330 men contracted HIV through sex between men and 247 men through heterosexual intercourse in Finland during the period 2000-2007.

"It is estimated that some 5 percent of all men have had sexual contacts with other men, which makes the risk of recent HIV infection through sex between men about 25-fold compared with that in heterosexual relationships. The selection of blood donors is largely based on assessment of risks in various donor groups and less so on individual risk behaviour." (Sources: NewsRoom Finland, 6/30/08; Ombudsman Statement, 6/30/08; Finnish Red Cross release, 6/30/08)

AMA Statement (continued from page 2)

As for a one-year deferral, the AMA said "while the increased risk with a one-year abstinence from blood donation from the last MSM contact would be very small, it is not zero. This small but scientifically real increase in risk represents a clear violation of ethical principles and therefore is not tolerable. If a 5- or 10-year deferral policy is considered, risk management calculations would yield risks at a level that many might consider acceptable."

The AMA had considered other language pointing out the weaknesses of current risk assessment models and a recommendation to ask the AMA Ethical and Judicial Council to examine the societal and ethical impacts of moving to a five-year deferral.

But the organization concluded that the data and explanations offered in the report itself, combined with the discussion at the hearing, supported a decision to remove the wording relating to the weakness of the models. The House of Delegates also removed the second recommendation of the report because the issue at hand was a risk- and science-based decision and further ethical scrutiny by the Council was deemed unnecessary. The Council's examination of any issue is always science-based, while any consideration of the ethical impact of a change in policy for MSM would be based, at least in part, on societal values, the AMA said. The AMA statement can be found at www.ama-assn.org/ama/pub/category/18644.html ♦

# 医薬品 研究報告 調査報告書

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| 販売名(企業名) | 合成血-LR「日赤」(日本赤十字社)<br>照射合成血-LR「日赤」(日本赤十字社) | | | |

**研究報告の概要**

○米国における供血者の*Tripanosoma Cruzi*(*T. cruzi*)スクリーニング10ヶ月間の経験:検出頻度、リスク要因、費用対効果

背景:供血者の*T. Cruzi*スクリーニングは血液の安全性を高めるが、財政的な負担と潜在的な供血者損失の原因ともなり得る。ここでは、米国の全供血者を対象に*T. cruzi*検査が導入された2007年1月30日以降、10ヶ月間の経験を報告する。

方法:供血者は、供血前の問診の際に、出生国と*T. cruzi*流行地の中南米で過ごした期間についての質問に回答した。ELISA法で*T. cruzi*繰り返し陽性(RR)となった供血者は通知を受け、シャーガス病のリスク要因と症状についてのインタビューに回答した。ELISA RRの供血はRIPAで確認試験を行った。また、費用対効果分析によって全供血者対象の*T. cruzi*スクリーニングの医療経済的な面を検討した。

結果:約652,000名の供血適格者のうち、リピートドナーの2.1%、初回ドナーの4.8%が、問診で中南米に3ヵ月以上の滞在歴があると回答した。期間中に93名(うち3名は自己血ドナー)が*T. cruzi* RRとなった。適合血供血のRR発生率は0.0138% (90/651,471; 1:7,239)だった。RRの供血のうちRIPA陽性は34% (28/82)、陽性確認率は特異度99.99%で0.0043% (1:23,267)だった。リスク要因としては、中南米の農村部居住歴、わらぶき屋根や泥の壁の家の居住歴、母方の家族が中南米出身、などが報告された。シャーガス病関連の症状を報告した人の割合は、RIPA陽性及び陰性供血者で同程度だったが、無症候のドナーはそれよりも多く、ELISA RRの供血者でも20%では症状が報告されなかった。予備的費用対効果分析では、スクリーニングはスクリーニング未実施と比較して$10,000,000/QALYを超える費用効果であることが示された。

結論:*T. cruzi*感染のリスク要因発現率は、検査前の予想と同程度だった。RR供血の大半はRIPAで陰性だったが、ELISAの特異度は、供血者損失と比較して良好だった。RIPA陽性の供血者は地理的な暴露リスクを報告したが、シャーガス病関連の症状を報告した人は少数だった。症状に関連した質問は、別の疾患で同じ症状を発症する場合があるため、地理的なリスク要因の質問よりも有益ではないと考えられた。全供血のスクリーニングは費用対効果が低く、出生地と初回供血者に対象を絞った対策の検討が示唆された。

| 報告企業の意見 | 今後の対応 |
|---|---|
| 米国の供血者を対象にT. cruzi検査が導入された後10ヶ月間で、陽性確認率は0.0043%だった。症状に関連した質問は地理的なリスク要因の質問よりも有益ではないと考えられること、全供血のスクリーニングは費用対効果が低く、出生地と初回供血者に対象を絞ったスクリーニング戦略の検討が示唆されたとの報告である。 | 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、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。日本在住の中南米出身献血者については、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」班と共同して検討する予定である。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

# S19 - Emerging Infections

3C-S19-01

## 10-MONTH EXPERIENCE SCREENING USA BLOOD DONORS FOR *TRYPANOSOMA CRUZI*: YIELD, RISK FACTORS, AND COST EFFECTIVENESS

Custer S[1], Kamel HT[2], Tomasulo PA[2], Murphy EL[3], Busch MP[1]
[1]*Blood Systems Research Institute, San Francisco, USA* [2]*Blood Systems Inc., Scottsdale, AZ, USA* [3]*University of California, San Franscisco, CA, USA*

Background: Screening blood donors for the parasite *Trypanosoma cruzi*, the cause of Chagas disease, can improve transfusion safety but may come at a high price financially and potentially in donors lost. Since January 30, 2007 all donors have been tested for *T. cruzi* by an USA FDA-approved ELISA. Here we report our experience during the first 10 months of testing and interviewing donors.

Methods: Donors complete a pre-donation health questionnaire that includes questions on country of birth and time spent in Mexico, Central and South America, areas endemic for *T. cruzi*. Donors who test ELISA repeat reactive (RR) for *T. cruzi* are informed by telephone and asked to complete an interview to assess risk factors for and symptoms of Chagas disease. ELISA RR donations are tested by radioimmunoprecipitation assay (RIPA) to discriminate confirmed- from false-positive results. We also conducted a cost-effectiveness analysis to assess the health economics of universal donor screening for *T. cruzi* in the USA using an updated version of a published model [].

Results: Of nearly 652;000 eligible allogeneic donors, 2.1% of repeat donors and 4.8% of first-time donors report having spent 3 months or more in Latin America based on pre-donation questions. 93 donors (including 3 autologous donors) tested T cruzi RR in the first 10 months of testing. The RR rate for allogeneic donations was 0.0138% (90/651;471; 1:7239). Only 34% (28 of 82 tested to date) RR donations tested RIPA-positive, for a confirmed yield of 0.0043% (1:23,267) with a specificity of 99.99%. The yield of RIPA-positive donations according to region of birth is provided in the table.

Reported risk factors include previously living in rural areas of Latin America, living in housing with thatched roofs and/or mud walls, and maternal family history in Latin America. RIPA-positive and negative donors reported similar frequencies of symptoms that could indicate Chagas disease, yet no symptom was reported by more that 20% of ELISA RR donors. Preliminary cost effectiveness analysis comparing no screening to screening using ELISA and supplemental RIPA indicated a cost-effectiveness of >$10,000,000/QALY.

| Birth country or region | RIPA positive prevalence |
|---|---|
| USA | 1:108,207 |
| Mexico | 1:1800 |
| Central or South America | 1:154 |
| All other countries | 1:13,410 |
| Missing/Unknown | 1:82,485 |

Conclusion: The prevalence of and risk factors for *T. cruzi* infection are consistent with pre-testing expectations. Although the majority of RR donations did not test RIPA-positive, the specificity of the ELISA was good with substantial donor loss not evident. RIPA-reactive donors have reported geographical exposure risks and a small number have indicated symptoms consistent with Chagas disease. Symptom-related questions appear less valuable for targeting screening than geographic risk factor questions due to the potential for other health conditions to cause the same symptoms. The cost-effectiveness of screening all donations is poor and may represent an extremely inefficient use of resources, indicating that targeted screening strategies focused on country of birth and first-time donor-status should be considered.

Reference: Wilson LS, Strosberg AM, Barrio K. Cost-effectiveness of Chagas disease interventions in latin America and the Caribbean: Markov models. Am J Trop Med Hyg 2005; 73: 901–910.

3C-S19-02

## EVALUATING THE EFFECTIVENESS OF MALARIA DEFERRALS THROUGH ANTIBODY TESTING

Leiby D, Nguyen L, Goff T, Gibble J
*American Red Cross, Rockville, MD, USA*

Background: For decades US blood collection organizations have used risk-factor questions to defer donors deemed to be at-risk for infection with *Plasmodium* spp., the etiologic agents of malaria. Risk factors are broadly classified as travel to or residence in a Plasmodium-endemic country, or past history of malaria. Affirmative responses to any one these risk-factor questions results in deferral from donating blood for 1–3 years. In recent years it has become clear that this approach has a negative impact on blood availability. Despite < 5 cases of transfusion-transmitted malaria in the US since 1998, over 100,000 potential donors are lost to malaria related deferrals each year. Thus, malaria can now viewed primarily as a blood availability issue, as opposed to a blood safety issue.

Aim: Assess the effectiveness of current malaria risk-factor questions by testing groups of deferred and non-deferred donors.

Methods: Blood donors previously deferred for malaria risk, defined as travel to or residence in *Plasmodium* spp. endemic areas or a prior history of malaria, were recruited and enrolled in the present study following administration of consent. Each study subject provided 10 ml of blood (EDTA) and completed a detailed questionnaire regarding risk factors for exposure to *Plasmodium* spp. Blood samples were tested by EIA (NewMarket Laboratories, UK) for *Plasmodium* spp. antibodies as per the manufacturers' instructions. Those samples found to be repeat reactive by EIA were considered positive and tested by real-time PCR for the presence of parasite DNA, and subsequent speciation. In addition, a group of randomly selected, non-deferred donors was selected and tested to determine assay specificity.

Results: A total of 1473 deferred donors enrolled in the study and provided a blood sample for EIA testing. Among those tested, 21 (1.43%) were initially reactive and 20 (1.36%) were repeat reactive. All samples tested by real-time PCR were negative for parasite DNA. The distribution of the 20 repeat reactive donors among the deferral categories was as follows: 14 for travel, 5 for residency and 1 for malaria history. The results of the risk factor questionnaire revealed that most seropositive donors had multiple risk factors including 17 (85%) with either residence in an endemic country or a past history of malaria. A group of non-deferred donors (n = 3229) was also tested by EIA and 21 (0.65%) were initially reactive and 11 (0.34%) were repeat reactive. Four of these 11 had a past history of malaria and three others had spent extensive time in *Plasmodium*-endemic countries.

Conclusions: Blood donors seropositive for *Plasmodium* spp. were detected among non-deferred and deferred donors. The relationship between long-term antibody titers and the risk for transmitting infection remains unclear, but semi-immune donors have been implicated in transfusion cases previously. The current approach to donor deferral is inconsistent, failing to defer donors with residence in endemic areas and/or a past history of malaria, two factors shown to be associated with transfusion transmission. In contrast, excessive donor deferral for travel to Latin America produces unnecessary donor loss, despite minimal risk for transmitting infection.

3C-S19-03

## GENETIC VARIABILITY OF WEST NILE VIRUS (WNV) IN CLINICAL ISOLATES FROM US

Rios M, Grinev A, Chancey C, Daniel S, Rios M
*Food and Drug Administration, Bethesda, MD, USA*

Background: WNV is endemic in the US and has caused 1.5–3.5 million human infections since 1999, with >1000 cases of neurological diseases and ≥100 deaths yearly since 2002. WNV is transmissible by transfusion

 

# 医薬品 研究報告 調査報告書

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| 販売名(企業名) | 合成血-LR「日赤」(日本赤十字社)<br>照射合成血-LR「日赤」(日本赤十字社) | | Walderhaug M, Menis M. XXIIXth Congress of the International Society of Blood Transfusion; 2008 Jun 7-12; Macao. | 米国 |

**研究報告の概要**

○パンデミックインフルエンザが米国の血液供給に与える影響のシミュレーション
米国におけるパンデミックインフルエンザ発生に備えて、パンデミックによる供血の減少と製造担当職員の不足により、供血数と職員数が通常程度に回復する前に在庫がなくなる可能性を分析した。米国では、年間約1450万製剤分の供血が行われ、約530万件の輸血が行われている。パンデミック中に起こりうるシナリオを検証するために、米国の血液供給量、1日当たりの供血数、1日当たりの需要について、個々にコンピュータシミュレーションを行った。シミュレーションは、製剤に関しては「先入れ先出し」法で行い、各製剤の供血後の日数の経過を追った。1日のシミュレーションで保存期間が42日を超えた製剤は供給から排除された。1日当たりの供血数については、供血記録から得られた通常の供給量と標準的逸脱数に基づく確率的シミュレーションを行った。1日当たりの需要のデータは、米国メディケア&メディケイドサービス由来の、65歳以上の入院患者の1日当たりの輸血実施数に関するデータと同様の方法で算定した。1日当たりの供血数と血液需要に関する分析は、1週間のうち日曜日の供血と需要が最も少なく、週半ばが最も多いというパターンを示した。1日の血液供給のシミュレーションを複数年分続けた場合では、血液供給量の見積もりは夏に減少し冬に回復するパターンを示した。パンデミックインフルエンザの影響を検証するため、3ヶ月間の供血量が50%減少したとしてシミュレーションを行ったところ、血液需要に何も制限がない場合は、血液供給量のほとんどを使い尽くした。しかし、血液の使用を必要最低限に制限した場合は、3ヶ月間供血が減少した場合でも血液在庫がなくなることはなかった。このシミュレーションモデルは、実際の血液供給量に関して適切であり、パンデミックインフルエンザ中に考えられるシナリオの範囲を策定する際に有用と考えられる結果を導き出した。

| 報告企業の意見 | 今後の対応 |
|---|---|
| 米国におけるパンデミックインフルエンザのシミュレーションで、3ヶ月間の血液供血量が50%減少した場合、血液需要に制限がない場合は血液在庫のほとんどを使い尽くしたが、血液の使用を必要最低限に制限した場合は血液在庫がなくなることはなかったとの報告である。日本赤十字社では家禽に高病原性トリインフルエンザの流行が認められた場合、当該飼養農場の関係者や防疫作業従事者の献血制限を行っている。 | 日本においてもパンデミックインフルエンザの発生が予期されることから、安全な血液の安定供給を確保し血液事業を継続するための対応計画を検討する必要がある。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

and since 2003 blood donations are screened for WNV RNA. Investigation of WNV genetic variation is important since persistent reoccurrence suggests viral adaptation through mutations that can potentially interfere with diagnostic and screening assays, pathogenesis and therapeutic approaches. This study reports the genomic variation of WNV observed in 67 clinical isolates obtained in the continental US during 6 consecutive years (2002–2007).

Methods: RNA extracts were prepared from WNV and subjected to RT-PCR and sequencing. Sequences were compared to the prototype WN-NY99 and other isolates previously studied using NTI Vector. We also developed and validated a multiplex RT-PCR assay to investigate if the newly identified deletion found in ID was also observed in other states. All specimens were tested for WNV 3'UTR deletion using this assay.

Results: Sequence results from 16 complete genomic sequences revealed 20–48 nucleotide (nt) mutations compared to the prototype WN-NY99. We observed an increase of a nucleotide divergence in the full WNV genomes from 0.18% in 2002 to 0.48% in 2006. It should be noted that 80% of the nt changes in structural regions are transitions (U ' C) and 75% are silent mutations. Twelve new mutations identified in 2005, became fixed in 2006. The 2006 and 2007 isolates shared three amino acid substitutions (Val449Ala, Ala2209Thr and Lys2842Arg), but most nt changes are silent transitions (U ' C, A'G). A 13-nt deletion in the 3'NCR (10414–10426) was identified in isolates from Idaho (ID-Δ13). Further investigation of 47 isolates from 2006 and 2007 for ID-Δ13, showed geographical localization of this variant as observed in 12/25 (48%) of isolates from ID, and in one 2006 isolate from ND. The new ID-Δ13 variant of WNV became fixed in 2007.

Conclusion: In this study we report the emergence of a new genetic variant of WNV carrying a 13-nt deletion at the 3'NCR (WNV-ID-Δ13), found in Idaho. The 3'NCR is known to be critical for WNV replication, however WNV-ID-Δ13 grows well in Vero cell cultures, but preliminary study showed steady replication efficiency and normal plaque in Vero cells. The impact of ID-Δ13 in viral pathogenesis is under investigation. Nucleotide sequence alignments indicate that, most new mutations are not fixed, but WNV has continued to diverge and the number of fixed mutations as well as overall genetic divergence has significantly increased. Surveillance for genetic variation is essential to assure public health since emergence of mutants could potentially decrease sensitivity of screening and diagnostic assays, affect viral pathogenesis, and negatively impact the efficacy of vaccines and the development of specific therapies.

### 3C-S19-04
## SCREENING OF BLOOD DONORS FOR CHIKUNGUNYA VIRUS – DEVELOPMENT AND EVALUATION OF MINIPOOL-NAT AND ANTIBODY TESTS

Schmidt M[1], Hourfar MK[1], Drosten C[2], Seifried E, Panning M[2]
[1]*German Red Cross, Institute Frankfurt, Frankfurt am Main, Germany*
[2]*Institute of Virology, University of Bonn Medical Centre, Bonn, Germany*

Background: The outbreak of Chikungunya fever in the southeastern islands of the Indian Ocean has drawn the attention of the transfusion community to Chikungunya virus. The virus has now spread to India and wide parts of Southeast Asia. Additionally many infections in European travellers returning from these regions to their home countries have been reported. Chikungunya virus can cause a wide spectrum of disease which may range from no or mild symptoms to death. It is known to be spread by blood in symptomatic cases and likely it could be spread by transfusion and transplantation of organs from people with pre-symptomatic or asymptomatic disease. Adequate screening procedures to identify viremic donations, however, were not available until now.

Methods: A real-time minipool NAT assay for the current epidemic strain of Chikungunya virus was used on a total of 29,568 blood donor samples, tested in minipools of up to 96 donations. To validate the sensitivity of the assay, routine donor minipools were spiked with inactivated virus and were used as positive controls. Additional to NAT-testing 9600 blood donations were screened for IgG-antibodies against Chikungunya virus to determine the prevalence of the infection in our blood donor population. Plasma samples from symptomatic Chikungunya virus infected travellers were analyzed for virus-load and antibody status.

Results: By testing 9600 blood donations for Chikungunya-specific IgG-antibodies no reactive donation was detected. Likewise, no viremic donation was identified by screening 29,568 clinically asymptomatic blood donors by minipool-NAT. The minipool-NAT assay provided sufficient sensitivity to detect plasma samples from symptomatic patients infected with the pathogen. It can be expected that the assay is also capable to detect viremic donations from pre-symptomatic or asymptomatic donors. This is because it was found that virus load in Chikungunya virus infected travellers was highest with onset of symptoms (day 0). After day 7 after onset of symptoms no Chikungunya virus RNA was found in symptomatic travellers. Specificity of the assay was 100% because none of the tested blood donors were found to be positive for the reemerged Alphavirus.

Discussion: Although no donation infected with Chikungunya virus has been identified among the donors subject to our study it is accepted that the reemerged pathogen poses a risk for recipients of blood products - in particular for immunocompromized patients. A recent outbreak of Chikungunya virus in Italy has shown that this virus also poses a risk to countries of the western hemisphere if competent vectors are prevalent. With the assay described for the first time highly sensitive screening of blood-donations on a routine basis is feasible. Since as no approved inactivation procedures exist for red blood cells exist, screening for viremic donations may be the method of choice in order to guarantee safe blood products in countries affected by the Chikungunya epidemic.

### 3C-S19-05
## SIMULATING THE IMPACT OF PANDEMIC INFLUENZA ON THE US BLOOD SUPPLY

Walderhaug M, Menis M
*US Food & Drug Administration, Rockville, MD, USA*

In order to prepare for a possible pandemic influenza event in the US, we investigated the potential for reduced donations and blood-processing staff shortages due to an influenza pandemic to exhaust blood stocks before normal donations and staff levels are restored. Approximately 14.5 million units of blood are collected annually in the US and approximately 5.3 million receive blood transfusions per year. To examine a range of potential scenarios that might occur during a pandemic, we developed a discrete event computer simulation of the estimated aggregate US blood supply, daily blood donations, and daily demand. The simulation used a 'first in, first out' rule with respect to blood units, and kept track of the number of days post collection of each simulated blood unit. During a day's simulation any units older than 42 days were eliminated from the aggregate supply. Daily blood donations were probabilistically simulated based on a normal distribution of means and standard deviations obtained from donation records. Daily blood demand data were estimated in a similar manner based on multiple years of U.S. Centers for Medicare & Medicaid Services (CMS) MedPAR derived data on the daily number of inpatient blood transfusion procedures recorded for elderly patients 65 years old and over. An analysis of daily donations and blood demand showed similar patterns through the week with the least amount of donations and demand on Sunday with peak donations and demand at mid-week. Simulating the daily blood supply for multiple years in simulation showed the estimated aggregate blood supply behavior was similar to observed patterns of blood supply levels in the US specifically, showing a decline in overall levels during the summer followed by a recovery of levels in the winter. To examine the impact of pandemic influenza, a 50% decline in blood donations for 3 months was simulated, and the effect was a depletion most of the aggregate blood supply, if no limitation of blood demand was applied; however, if blood demand is limited to essential uses, then a three month period of reduced donations can be endured despite a significant depletion of aggregate blood stocks. The simulation model provided results that appear to be reasonable with respect to observed estimates of aggregate blood supply and to be useful in exploring a range of possible scenarios expected during pandemic influenza.

 