living conditions. Half the population included arrived in Spain after 2000, a fact that illustrates the increasing immigration rates from Latin America observed over the past years. Another interesting result from the questionnaire was that the information obtained about living conditions in the Chagas disease endemic area (rural area, adobe house) did not correlate with the presence or absence of antibodies to *T. cruzi*. People born in endemic regions (7 of 11 positive donors) generally declared that they had never lived in a rural environment or an adobe house (Table 2), as is commonly assumed. Hence, this question is not useful for differentiation purposes. Interestingly, the same conclusion was drawn from the Berlin study, in which 95 of 100 immigrants declared that they came from an urban area, including the 5 cases of confirmed Chagas disease.[21]

The two serologic assays used in this study were chosen because at the beginning of the study they were commercially available and EC-marketed. Both are based on recombinant antigens, whereas the third conventional in-house ELISA is based on whole parasite lysate. All samples confirmed as positive had been initially reactive with both recombinant antigens assays, and all samples initially reactive with only one assay presented a nonreactive result in the in-house ELISA and were considered false-positive samples. It is worth noting that many discrepant results observed between both assays corresponded to low 0.9 to 1 signal-to-cutoff rates for bioelisa Chagas (Biokit) or doubtful reactions with ID-PaGIA (DiaMed), which were all considered as initially reactive in this study. Additionally, it should be mentioned that the *T. cruzi* ELISA test system performed on all initially reactive samples (with one or two tests) confirmed the results obtained with the conventional in-house ELISA. The high rate of inconclusive or false-positive results obtained when one diagnostic test is used underscores the need to confirm all initially positive results with a second serologic technique. In any case, there is still a need for a real confirmatory test to overcome the issues of discrepancies and false results (positive or negative). The ID-PaGIA assay allows testing of a small number of samples at a time. Although this system has the drawback of rather subjective reading, it could be useful in blood centers with a small volume of donations and is now even more reliable since a third antigen has been recently added to increase the sensitivity of the test. The ELISA format, which allows for automation and objective reading, should be indicated in other blood centers. An even more appropriate strategy would be the use of two screening tests, one based on recombinant antigens and the other on crude antigens.[20]

In summary, this study reports a seroprevalence of *T. cruzi* infection of 0.62 percent among at-risk donors in Catalonia and emphasizes the need to include individuals who have resided in, but were not necessarily born in endemic areas as at-risk donors. The difficulty of this type of selective screening is proper identification of the risk population, which essentially depends on the predonation interview. Latin Americans accounted for more than 1 percent of the total of donors in our study, and this substantial contribution underscores the need to accept them as donors.

In the future, techniques to inactivate or reduce the parasite load, which are currently under development or evaluation,[29,30] might be applicable to blood components. At this time, however, detection of *T. cruzi* infection is the only preventive measure available to accept at-risk blood donors.

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別紙様式第2-1

No. 33

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	総合機構処理欄
				2008. 10. 15	該当なし	

一般的名称	人全血液	研究報告の公表状況	BuaNews online, Mon 13 Oct 2008. available at http://www.buanews.gov.za/news/08/08101311151006	公表国 南アフリカ
販売名(企業名)	人全血液-LR「日赤」(日本赤十字社) 照射人全血液-LR「日赤」(日本赤十字社)			

研究報告の概要

○アレナウイルスと特定された未知の疾患
南アフリカ、ヨハネスブルグで3名の死者を出したウイルスは、暫定的に西アフリカのラッサウイルスに近い、齧歯類媒介性アレナウイルスであると特定された。ウイルスは感染マウスの排泄物を介し、人間の食物やハウスダストを汚染する可能性がある。
南アフリカ国立感染症研究所(NICD)と保健省は共同で、このウイルスが体液を介してヒトからヒトに感染するため、「患者の看護に特別な予防的措置が必要である」との声明を発表した。3名の死因を確定するには更なる検査が必要である。新たなアレナウイルスであるかどうか、ならびに当該ウイルスの分布について検討を行う必要がある。ヒトに疾患を引き起こすアレナウイルスが南アフリカの齧歯類に存在することはまだ示されていないとNICDは述べた。
1人目の女性患者は、9月中旬に重篤な容態でザンビアから搬送され、Morningside Medi-Clinicに入院し、2日後に死亡した。約2週間後、1人目の患者の搬送に同行した救急救命士が死亡し、間もなく看護師が死亡した。
1人目の患者と接触した他の3名の患者は退院したことが確認されているが、依然として2名が厳重な監視下に置かれている。1名は、発熱およびインフルエンザ様症状を発症した救急救命士であり、もう1名は2人目の患者をケアした女性看護師である。彼女は、隔離され抗ウイルス剤ribavirinの投与を受けており、現在は安定している。

報告企業の意見	今後の対応
南アフリカ、ヨハネスブルグで3名の死者を出したウイルスは、暫定的に西アフリカのラッサウイルスに近い、齧歯類媒介性アレナウイルスであると特定されたとの報告である。	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。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

人全血液-LR「日赤」
照射人全血液-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

BuaNews ONLINE
www.buanews.gov.za

Compiled by the Government Communication and Information System
Date: 13 Oct 2008
Title: Unknown illness identified as Arenavirus

By Luyanda Makapela

Johannesburg - The virus which has caused the death of three people has been provisionally identified as the rodent-borne Arenavirus.

The Arenavirus, related to the Lassa Fever Virus of West Africa, causes chronic infections in multimammate mice. Infected mice's excretion contains the virus which can contaminate human food or house dust.

A joint statement by the National Institute for Communicable Disease (NICD) and the Department of Health explained that the Arenavirus is a disease spread from human to human through the contact of body fluids.

"Special precautions are required in nursing patients," a statement said.

The finding follows blood samples being sent to Atlanta, in the United States to determine the cause of the deaths of three people who had been suspected of contracting Viral Haemorrhagic Fever.

The virus is similar to Lassa Fever, the department said. It has previously been found in rodents elsewhere in Africa, *but has not been found to cause disease in humans other than in West Africa.*

Further tests are needed to confirm the diagnosis by growing the virus in culture.

"It needs to be determined whether it is a previously unrecognised member of the Areaviruses, and what its distribution is. There is no indication as yet that Arenaviruses which cause disease in humans are present in South African rodents," the NICD said.

The first victim, who had to be flown in from Zambia in a critical condition, was admitted to the Morningside Medi-Clinic in mid September. She died two days later.

About two weeks later, the paramedic who had flown in with the first victim, was admitted at the same clinic presenting the same symptoms.

A nurse, Gladys Mthembu died shortly afterwards. According to certain reports Ms Mthembu's family has been given a go-ahead to continue with the funeral arrangements as her bedroom had been cordoned off by health officials

Maria Mokubung, a cleaner at the Morningside Medi-Clinic, who also died last weekend has since been ruled out as a possible victim of the virus

Meanwhile the Gauteng Health Department has confirmed that the three other patients, including nurse's female supervisor, who had been under observation for showing symptoms of the virus have been discharged.

They had been in contact with the nurse who died.

However, departmental spokesperson Phumelele Kaunda said there were two contacts that were still under active surveillance after being admitted for observation.

The one patient is a paramedic who had contact with the first patient and developed fever and flu-like symptoms. He was admitted initially in Flora Clinic and then transferred to Morningside Medi-Clinic with a diagnosis of kidney stones.

The other patient is a nurse who attended to the second patient and developed signs and symptoms similar to the first three patients. She is being treated in isolation and received the anti-viral medication, ribavirin. The patient is presently stable.

Gauteng Health MEC Brian Hlongwa meanwhile has sent condolences to the families of those that were killed by the viral infection, particularly families of health professionals who died in the line of duty.

"This illustrates the dedication of our health professionals and the need to society to respect and honour the work that they do," said MEC Hlongwa.

He also thanked the NICD, the National Health Laboratory Service, Centre for Disease Control in Atlanta and the World Health Organisation for ensuring that the results were made available soon. - BuaNews

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 2008年10月20日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称	別紙のとおり	研究報告の公表状況	ProMED-mail, 20081028.3409	公表国 ザンビア・南アフリカ	
販売名（企業名）	別紙のとおり				

研究報告の概要

問題点：南アフリカにおいて、アレナウイルス科の新たなウイルスによる見られる感染により5人の患者が報告された。

初発患者(症例1)の発症は9/2日で、これに続いて3人の二次感染症例と1人の三次感染患者が報告された。初発患者と二次感染の3人は死亡し、三次感染症例は現在入院中である。患者の年齢層は33～47才、女性4人と男性1人。初発患者の感染源は判っていない。他の4人の患者は全員が医療施設内で、初発患者もしくは二次感染患者の血液・体液と接触があった可能性があった。初発患者はザンビア在住で、治療のための南アフリカへの移送後に死亡した。症例2は、症例1の移送に付き添った救急隊員の1人で、症例3は集中治療室にいた症例1の看護を担当していた。症例4は症例1が入院していた部屋の清掃を行った。症例5は症例2の看護を担当した。二次および三次感染患者の潜伏期間は7～13日と考えられている。死亡した4人の患者の発病から死亡までの期間は9～12日であった。患者全員が初発症状として発熱・筋肉痛・頭痛を伴うインフルエンザ様症状を示した。7日間で重症度が増し、いずれも下痢と咽頭痛が見られた。第6～8病日に顔面と躯幹の麻疹様発疹が報告されている。3人に顔面の浮腫があった。死亡した患者では、末期症状として呼吸困難・神経学的症状・循環不全を伴う突然で急速な状態の悪化が見られた。出血症状は著明な特徴ではないが、1人に皮下出血、もう1人は穿刺部位からの持続出血が見られた。暫定的な検査により、今回の感染はアレナウイルス科における新たな異なるウイルスと見られている。

現在(10/28日)まで新たな感染疑い症例は発生していない。感染流行は封じ込められたようであり、医療施設内環境下で濃厚接触者だけに感染が限定されている。病原体の詳細な特徴については、現在調査中であり、初発患者の感染源についての調査も必要である。症候性感染発生の可能性の検討も、感染流行の範囲や臨床像をより理解するために重要である。

報告企業の意見	今後の対応
別紙のとおり	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。

使用上の注意記載状況・その他参考事項等

記載なし

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	アレナウイルス属は、エンベロープをもつ1本鎖RNA(−)ウイルスである。齧歯類に寄生し、慢性腎臓感染をおこす。齧歯類の尿中は高ウイルス価であり、ヒトの食品やハウスダストを汚染する。曝露したヒトは偶発的宿主となる。このウイルスの原型はリンパ球性脈絡膜髄膜炎ウイルス（LCMV）であり、ヒトに感染するとインフルエンザ様症状、無菌性髄膜炎もしくは重症髄膜脳炎を発症する。出血熱症候群の原因となるArenavirusesは南米(New World arenaviruses)から数多く報告されている。いわゆるOld World arenavirusesは世界中に分布するLCMVと、西アフリカのナイジェリア、シエラレオネ、リベリア、ギニアを中心に1年間に最大50万人が感染し、実際にはさらに広い地域に分布すると見られているラッサ熱ウイルスである。ラッサ熱ウイルス感染の臨床症状としては、不顕性、軽症発熱性疾患から劇症出血性疾患まで様々であり、致死率は一般的な社会環境における1〜2%から、入院患者では20%、院内感染では40%以上に及ぶこともある。西アフリカ一帯に生息する野ネズミの一種であるマストミス（*Mastomys natalensis*）は、ラッサ熱ウイルスの最重要宿主であり、その分布は、西アフリカから東アフリカ一帯と、南アフリカ北東端まで南に広がっている。他のMastomys種とも分布域が重複し、アレナウイルスは過去にはアフリカ南部の齧歯類でも確認されている。 (http://www.forth.go.jp/cgi-bin/promed/search.cgi?title_link=20081029-0050&button_detail=on) 弊所の血漿分画製剤の製造工程には、冷エタノール分画工程、ウイルス除去膜ろ過工程あるいは加熱工程等の原理の異なるウイルス除去及び不活化工程が存在しているので、ウイルスクリアランスが期待される。 各製造工程のウイルス除去・不活化効果は、「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）」に従い、ウシウイルス性下痢ウイルス（BVDV）、仮性狂犬病ウイルス（PRV）、ブタパルボウイルス（PPV）、A型肝炎ウイルス（HAV）または脳心筋炎ウイルス（EMCV）をモデルウイルスとして、ウイルスプロセスバリデーションを実施し、評価を行っている。今回報告したアレナウイルス属は、エンベロープの有無、核酸の種類等からモデルウイルスとしてはBVDVが該当すると考えられるが、上記バリデーションの結果から、BVDVの除去・不活化効果を有することを確認している。 また、これまでに当該製剤によるアレナウイルス感染の報告例は無い。 以上の点から、当該製剤はアレナウイルスに対する安全性を確保していると考える。

*現在製造を行っていない

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UNDIAGNOSED FATALITIES - SOUTH AFRICA ex ZAMBIA (10): ARENAVIRUS
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Arena virus outbreak, South Africa — Update

This updates all previous reports and includes available data as of 24 Oct 2008. An outbreak of infection due to an arenavirus was identified in South Africa in early October 2008. A total of 5 cases has been reported for the period 12 Sep to 24 Oct 2008.

The primary case (case 1) had onset of illness on 2 Sep 2008. An additional 3 secondary cases (case 2, 3 and 4) and 1 tertiary case (case 5) have been confirmed to have an arenavirus infection by laboratory testing. The primary case and 3 secondary cases have died. The tertiary case is currently hospitalized. Ages of cases ranged from 33 to 47 years. 4 cases were female and 1 male. The source of infection is, as yet, unknown for the primary case. The other 4 cases all had potential exposure to blood and/or body fluids of a primary or secondary case in the health-care setting.

The primary case was a safari booking agent resident in Zambia. The patient was flown to South Africa for medical care in a critically ill condition on 12 Sep 2008, and died on 14 Sep 2008. Case 2 was a paramedic who cared for case 1 during the transfer from Zambia on 12 Sep 2008 and case 3 was a nurse who cared for case 1 in the intensive care unit from 12-14 Sep 2008. Case 2 was admitted on 27 Sep 2008 and died on 2 Oct 2008 and case 3 was admitted on 30 Sep 2008 and died on 5 Oct 2008. On 14 Sep 2008, case 4 performed terminal cleaning of the room in which case 1 was hospitalized. The 5th patient is a nurse who cared for case 2 from 27 Sep 2008 to 2 Oct 2008. She became ill on 9 Oct 2008 and is currently critical but stable. Ribavirin has been used for treatment in this case based on good evidence of efficacy in patients with Lassa fever (an arenavirus infection). The estimated incubation period (interval from exposure to symptom onset) in secondary and tertiary cases ranges from 7 to 13 days. In 4 patients who died, the interval from onset of illness to death ranged from 9 to 12 days (Figure 1).

Only limited clinical data are currently available for case 4, who presented late in the course of illness with bleeding and confusion and died soon thereafter. Clinical features of the remaining 4 cases, for which more clinical data were available, are presented. All patients presented initially with a non-specific flu-like illness with symptoms of fever, headache and myalgia. The illness increased in severity over 7 days with all 4 patients developing diarrhoea and pharyngitis during the course of illness. A morbiliform rash on the face and trunk was reported in 4 cases on day 6 - 8 of illness. Facial swelling occurred in 3 patients. There appeared to be an initial clinical improvement after hospital admission in 3 patients, followed by clinical deterioration. Sudden and rapid deterioration

with respiratory distress, neurological signs and circulatory collapse were terminal features in all patients who died. Bleeding was not a prominent feature. However, one patient had a petechial rash and another had oozing of blood from venepuncture sites. Chest pain was reported in case 1.

At the time of admission all patients had thrombocytopenia (range: 42–104 X109/L). Liver transaminases (AST and ALT) were available for 4 of 5 cases and were variable at the time of admission, however all 4 patients had raised AST and ALT during the course of their illness. Leucopenia was present on admission in 2 patients and 3 patients had a normal white blood cell count on admission. 4 patients subsequently developed leucocytosis during the course of hospitalisation. All contacts (family members, friends and healthcare staff) are being monitored with twice daily temperature measurements for a period of 21 days after the last exposure to a known case. In addition, safe burial of the deceased has been supervised by environmental health officers. Full personal protective equipment (PPE) and isolation precautions as per VHF protocols have been instituted.

The causative agent in this outbreak was initially identified as an Old World arenavirus by immunohistochemical tests performed at the Infectious Diseases Pathology Branch of the Centers for Disease Control and Prevention in Atlanta, USA, and on autopsy liver and skin samples taken with biopsy needles and skin punches in the Special Pathogens Unit of the National Institute for Communicable Diseases, National Health Laboratory Service, Sandringham (SPU–NICD/ NHLS), South Africa, from cases 2 and 3 on 9 Oct 2008 under biosafety level 4 laboratory conditions. Subsequently, infection with an Old World arenavirus has been confirmed in all 5 cases by positive PCR results and virus isolation by SPUNICD/ NHLS and CDC. Analysis of sequencing data generated at SPU–NICD/NHLS, Columbia University, New York, and CDC, Atlanta appears to indicate that the current outbreak is caused by a unique Old World arenavirus.

There are currently no additional suspected cases. The outbreak appears to be contained and has been confined to individuals with very close contact in a health–care setting. Monitoring of contacts, active case finding and investigation and management of suspected cases will continue as needed. Further characterization of the causative agent is under way and investigation into the source of infection in the primary case is required. Additional studies to determine whether mild/asymptomatic infection occurred amongst close contacts and other exposed individuals would be essential in better characterizing the extent of this outbreak and clinical spectrum of disease.

Arenaviruses are a family of enveloped negative sense single–stranded RNA viruses. Members of the family are parasites of rodents, in which they establish chronic renal infection. High titres of virus are present in rodent urine, which can contaminate human food or house dust. Exposed humans may become infected as accidental hosts. The prototype of the family is lymphocytic choriomeningitis (LCM) virus and infection of humans with this virus may present as an influenza–like illness, aseptic meningitis or severe meningo–encephalomyelitis. Arenaviruses which cause a haemorrhagic fever syndrome are well documented in South America (New World arenaviruses, including Junin, Machupo, Sabia and Guanarito viruses). The so–called Old World arenaviruses include LCM which in fact has a worldwide distribution, and Lassa fever virus which affects up to 500 000 people annually in West Africa, specifically in Nigeria, Sierra Leone, Liberia and Guinea, but the virus is suspected to be more widely distributed in that region.

The clinical spectrum of Lassa fever virus infection ranges from inapparent, through mild febrile illness to fulminant haemorrhagic disease, and mortality rates vary from 1–2 percent among cases in the community at large, through 20 percent among hospitalized patients, to >40 percent in nosocomial outbreaks. The multimammate mouse (Mastomys natalensis), which is the most important host of Lassa fever virus, has a distribution extending from West Africa across to East Africa and from there southwards to the northeasternmcorner of South Africa. Its distribution overlaps with that of other Mastomys species, and arenaviruses have been found in southern African rodents in the past, but there has been no previous association of these viruses with human disease despite sustained monitoring. Preliminary

testing indicates that the virus associated with the present nosocomial disease outbreak is a distinct new member of the family.

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[This update provides a definitive account of the recent outbreak of arenavirus-associated disease in South Africa. A primary case (case 1) had onset of illness on 2 Sep 2008. An additional 3 secondary cases (case 2, 3 and 4) and 1 tertiary case (case 5) have been confirmed to have an arenavirus infection by laboratory testing. Case 5 (not previously reported) is a nurse who cared for case 2 from 27 Sep 2008 to 2 Oct 2008. She became ill on 9 Oct 2008 and is currently critical but stable. Cases 1, 2, 3 and 4 did not survive infection.

Infection with an Old World arenavirus has been confirmed in all 5 cases by positive PCR results and virus isolation by SPUNICD/ NHLS and CDC. Analysis of sequencing data generated at SPU-NICD/NHLS, Columbia University, New York, and CDC, Atlanta, appears to indicate that the current outbreak is caused by a unique Old World arenavirus.

There are currently no additional suspected cases. The outbreak appears to be contained and has been confined to individuals with very close contact in a health-care setting. Monitoring of contacts, active case finding and investigation and management of suspected cases are continuing. Further characterization of the causative agent is under way, as is investigation into the source of infection in the primary case.
- Mod.CP]

[see also:
Undiagnosed fatalities - S. Africa ex Zambia (09): arenavirus 20081018.3300
Undiagnosed fatalities - S. Africa ex Zambia (08): arenavirus 20081013.3241]
Undiagnosed fatalities - S. Africa ex Zambia (07): arenavirus 20081012.3234
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Undiagnosed fatalities - South Africa ex Zambia (05) 20081008.3192
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