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
				2006. 7. 3	該当なし	

一般的名称	(製造承認書に記載なし)	研究報告の公表状況	ProMED. 20060624-1758, 2006 Jun 24. 情報源:Kyrgyzstan Press, 2006 Jun 22.	公表国 キルギスタン
販売名(企業名)	合成血「日赤」(日本赤十字社) 照射合成血「日赤」(日本赤十字社)			

研究報告の概要

○マラリアーキルギスタン
キルギスタンの首都で79例のマラリア症例が登録された。60例はBishkek地方、19例はChuysk地方の症例だった。予防手段を講じているにもかかわらず、流行は拡大中である。以下の情報はBishkekにある国立衛生疫学監視センター副所長のAdilbek Djuzenovから提供された。マラリア撲滅のための予防活動には数年必要である。キルギスタンでは2005年に125例の症例が登録された。このうちほとんどはBishkek地方のAk-Bata村とKalis ordo村の住民だった。感染の中心は、Chuysk地方のAla-Archinsk貯水池である。Ak-Bata村とKalis ordo村の819世帯で殺虫剤を散布した。しかし、住民に問題を理解させるのは困難で、殺虫剤散布も時々散布が許されるだけである。マラリア治療にはPrimosinが有効で、人道機関から十分な量の薬が送られている。
キルギスタンにおけるマラリアは、1959年に一度撲滅されたものの、1986年以降は、アフガニスタンからの帰還兵が入国するのに伴って毎年国内で感染した症例が登録されている。

報告企業の意見	今後の対応
キルギスタンの首都で79例のマラリア症例が登録され、流行が拡大中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、帰国後4週間は献血不適としている。今後も引き続き、マラリア感染に関する新たな知見及び情報の収集、対応に努める。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「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

Back

Archive Number 20060624.1758
Published Date 24-JUN-2006
Subject PRO/EDR> Malaria - Kyrgyzstan (Bishkek)

MALARIA - KYRGYZSTAN (BISHKEK)
****
A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases
<http://www.isid.org>

Date: Sat, 24 Jun 2006
From: ProMED-mail Russian correspondent AP <promed@promedmail.org>
Source: Kyrgyzstan Press [22 Jun 2006; trans. Mod.NR; edited]
<http://pr.kg/n/detail.php?id=3D8576>

In the capital of Kyrgyzstan 79 cases of malaria have been registered; 60 from Bishkek and 19 from the Chuysk region. Despite preventive measures, the outbreak is growing. This information was provided by the deputy chief of the state sanitary epidemiological surveillance (SES) center in Bishkek, Adilbek Djuzenov.

According to Adilbek Djuzenov, it requires several years of preventive work to destroy a malaria focus. Kyrgyzstan registered 125 malaria cases in 2005, of whom most were inhabitants of Ak-Bata and Kalis Ordo villages of Bishkek. The epicenter of the spread is the Ala-Archinsk reservoir in the Chuysk region.

According to Djuzenov, 819 households at Ak-Bata and Kalis ordo have been sprayed with insecticides. However, it is challenging for the population to understand the problem, and [only] sometimes do people allow the SES staff to spray their houses.

According to Adilbek Djuzenov, the disease can be treated with Primosin [ProMED does not know what drug is being referred to under this brand name], and enough drugs were delivered by humanitarian aid.

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ProMED-mail
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[ProMED reported 88 cases of malaria in Bishkek in 2005. We still do not have a species identification. Malaria was eradicated in Kyrgyzstan in 1959; however, from 1986 onwards, as a result of the importation of malaria by military personnel returning from Afghanistan, a few local cases have been registered annually. In 1986 and 1987, 14 and 10 autochthonous malaria cases were detected, respectively. In 1988, 21 cases due to local transmission were registered. In 2002, a total of 2267 autochthonous _P. vivax_ cases were reported in the southwestern regions of the country, including Batken, Osh and Jalal-Abad.

The explosive resumption of malaria transmission in Kyrgyzstan was the result of immigration of a number of infected people from Tajikistan into the Batken region. In 2004-2005, there was a significant decrease in the reported number of autochthonous malaria cases (42 in 2005). However, in 2004 the first autochthonous case of _P. falciparum_ malaria was reported in the Aravan district of the southern part of Kyrgyzstan, in an area bordering Uzbekistan, and in 2005 the number of autochthonous cases of _P. vivax_ malaria increased in the outskirts of Bishkek, the capital of the country (Source: <http://www.euro.who.int/malaria/ctryinfo/affected/20020712_17>).
ProMED reported 88 cases of malaria from Kyrgyzstan in 2005 in

contrast to the 42 the country reported theough WHO. This indicates that there may be some underreporting of cases. - Mod.EP]

[Bishkek is the capital of Kyrgyzstan and its population is 768 000. The Chuysk region borders Bishkek and has 765 700 people. - Mod.NR]

[A good map of Kyrgystan can be found at:
<http://www.lib.utexas.edu/maps/commonwealth/kyrgyzstan_pol96.jpg>. - Mod.MPP]

[see also:
2005

Malaria - Kyrgyzstan (02) 20050823.2489
Malaria - Kyrgyzstan 20050723.2124
2004

Malaria, falciparum - Kyrgyzstan (Osh) 20040815.2263
2002

Malaria, autochthonous - Russia (Moscow) 20020608.4439
2001

Malaria, autochthonous - NIS: 1992-2000 20010819.1962
2000

Malaria, autochthonous - Kazakhstan (02) 20000904.1507
Malaria, autochthonous - Russia (Krasnoyarsk) 20000816.1366
Malaria - Russia (Moscow) 20000525.0827
1999

Malaria, autochthonous - Russia (Ryazan) 19990909.1593
1998

Malaria - Turkmenistan (02) 19981218.2398
Malaria - Kyrgyzstan (02) 19980910.1825
Malaria - Azerbaijan & Newly Independent States 19980714.1332
Malaria, epidemic - Azerbaijan (02) 19980708.1278
Malaria, epidemic - Azerbaijan: RFI 19980706.1269]
.....nr/mpp/ep/pg/mpp

別紙様式第2-1

No. 7

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
				2006. 5. 24	該当なし	

一般的名称	(製造承認書に記載なし)	研究報告の公表状況	AABB Association Bulletin. 2006 Apr 26.	公表国 米国
販売名(企業名)	合成血「日赤」(日本赤十字社) 照射合成血「日赤」(日本赤十字社)			

研究報告の概要

○AABBがムンプスウイルスの流行に対応して採血施設に勧告
米国中西部でのムンプスの流行に対応して、AABBは感染者と感染者に接触した人を一時的に供血延期とすることを勧告した。輸血によるムンプスウイルスの感染はこれまで確認されていないが、ウイルス血症が起こることは知られている。このため、輸血による感染の可能性を考慮して、AABBの感染症委員会とFDAはムンプス流行地域の採血施設が予防策をとることに合意した。
採血施設への勧告の内容は以下の通りである。
・教育施設での移動採血を実施するかどうか、地元自治体や州の公衆衛生当局に照会すること。
・供血が見込まれる人に対して、疾患についての情報提供を行うこと。
・最近ムンプスに罹患した人については、すべての症状が消えてから14日間供血延期とすること。感染者と接触した人については、覚えている最後の接触から28日間延期すること。
・供血後にムンプスと診断された場合は、症状が消える前28日間および消えた後14日間の供血由来の製品は回収、隔離保管、廃棄を行うこと。供血後に感染者との接触が報告された場合は、覚えている最後の接触後28日間の供血由来の製品は回収、隔離保管、廃棄を行うこと。
・採血施設は、ムンプスが流行している施設あるいは地域での供血由来の新鮮凍結血漿については製造および使用を避け、他の製剤に転用してもよい。
受血者への通知については勧告していないが、輸血によるムンプスウイルス感染のリスクを推定するために行っても構わない。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「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

報告企業の意見	今後の対応
米国中西部でのムンプスの流行に対応して、AABBは感染者と感染者に接触した人を一時的に供血延期とすることを勧告したとの報告である。	日本赤十字社は、問診でムンプスの既往があった場合、治癒後3週間献血不可としている。献血後に感染が判明した場合は、今後も引き続き情報の収集に努める。

Advancing Transfusion and
Cellular Therapies Worldwide

ASSOCIATION BULLETIN

#06-04

Date: April 26, 2006

To: AABB Members

From: Christopher D. Hillyer, MD – President
Karen Shoos Lipton, JD – Chief Executive Officer

Re: Recommendations for Blood Collection Facilities in Response to Epidemic Mumps in the Midwest

Background

The state of Iowa is experiencing a large outbreak of mumps that began in December 2005. As of April 20, 2006 more than 1,000 suspect, probable and confirmed cases have been reported to the Iowa Department of Public Health. The majority of infections are among persons 18-25 years of age. Cases initially predominated in postsecondary educational facilities (colleges, universities, trade schools, etc). However, in recent weeks many cases have been reported outside these venues. Additional cases of mumps, possibly linked to the Iowa outbreak, are also under investigation in eight neighboring states, including Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, Nebraska and Wisconsin. The outbreak is expected to spread further, perhaps nationally.

The source of the current US outbreak is unknown. However, the mumps strain has been identified as serogroup G, the same as that circulating in the United Kingdom (UK). The outbreak in the UK has been ongoing from 2004 to 2006 and has involved more than 70,000 cases. The individuals had been fully immunized [with two doses of Measles-Mumps-Rubella (MMR) vaccine] in approximately 70% of the cases investigated to date.

Mumps is an acute viral infection characterized by a nonspecific prodrome including myalgia, anorexia, malaise, headache and fever, followed by acute onset of unilateral or bilateral tender swelling of parotid or other salivary glands. In unvaccinated populations, an estimated 30-70% of mumps infections are associated with typical acute parotitis. However, as many as 20% of infections are asymptomatic and nearly 50% are associated with nonspecific or primarily respiratory symptoms (cough, sore throat), with or without parotitis.

Complications of mumps infection can include deafness, orchitis, oophoritis, or mastitis (inflammation of the testicles, ovaries or breasts, respectively), pancreatitis,

meningitis/encephalitis and spontaneous abortion. With the exception of deafness, these complications are more common among adults than children.

Natural transmission of mumps virus occurs by direct contact with respiratory droplets (ie, coughing and sneezing), saliva or contact with contaminated fomites. The incubation period is generally 16-18 days (range 12-25 days) from exposure to onset of symptoms. Mumps can be spread from an infected person by droplets for about five days after onset of symptoms; however, virus has been found in the saliva of patients for as long as nine days after onset.

Members of the AABB Transfusion-Transmitted Diseases (TTD) Committee and representatives of the US Food and Drug Administration (FDA) have discussed the potential transfusion transmission of mumps to transfusion recipients from donors with unrecognized infection and asymptomatic viremia. Transfusion transmission of mumps virus has never been observed; however, viremia is known to occur, although the kinetics are poorly characterized. Information suggests that the viremia is in the form of both cell-associated and free virus. Whether transfusion-acquired disease would present with clinical signs that would allow recognition of mumps after transmission by this unnatural route is unknown.

Recommendations

On the basis of the current state of knowledge about the possibility of transfusion-transmitted mumps, the TTD Committee and the FDA agree that a precautionary approach should be adopted by blood collection facilities in areas affected by epidemic mumps until more information is available.

1. Blood drives at postsecondary educational facilities or other similar facilities in areas experiencing epidemic mumps should be scheduled or canceled at the discretion of the collection facility's medical director in consultation with local and/or state public health authorities. In making the decision, medical directors should use information about mumps activity in the general area and at the specific institution where the blood drive is scheduled. Decisions should be consistent with efforts to minimize the risk of the theoretical transmission of mumps yet maintain local and regional blood supplies adequate for medical need.
2. Donor information: Prospective donors in areas experiencing epidemic mumps should be provided with information about the existence of mumps in the local area, the concern about its theoretical transmission by blood, and the donor deferral criteria specified below. This information can be in any of the following forms:
    a. Information provided by recruiters before presentation to donate.
    b. Written information provided at registration that allows self-deferral before screening and/or during administration of the donor history questionnaire.
    c. New questions added to the donor history questionnaire to allow deferral at the time of screening.

These options are similar to those accepted by FDA at the time of the severe acute respiratory syndrome (SARS) epidemic. The decision to implement these measures in all

or part of a blood region should be made by the collection facility medical director in consultation with local and/or state public health authorities and using information about mumps activity in the area.

3. Donor eligibility: A donor is required to be well on the day of donation.
4. Temporary deferral criteria.
    a. Donors with recent mumps infection should be deferred until 14 days after the resolution of all symptoms of infection.
    b. Donors who have had contact with a person or persons with mumps should be deferred until 28 days after the last recognized contact. Contact is defined as any of the following situations:
        i. Living in the same dwelling (eg, house, apartment, dormitory room) as a case patient with a diagnosis of mumps.
        ii. Recognized direct contact with upper respiratory secretions (eg, kissing) or sharing utensils that might be contaminated with upper respiratory secretions (eg, eating utensils, cups, drinking glasses) with a case patient with a diagnosis of mumps.
        iii. Recognized contact within three feet of a case patient with a diagnosis of mumps without the use of barrier precautions (mask and eye protection).
    c. Per the AABB *Standards for Blood Banks and Transfusion Services, 23rd Edition,* receipt of MMR vaccination requires deferral for 28 days.
5. Post donation information: It is probable that if the epidemic is sustained, blood collection facilities will begin to receive post donation information about donors who have developed mumps or who have had recognized contact with mumps that had not been recognized and reported at the time of a prior donation. Because of the relatively long incubation period of mumps, there is a possibility that some of these donors may have been viremic at the time of their donation.
    a. When a donor provides post donation information that he or she has been diagnosed with mumps, the donor should be deferred for 14 days after resolution of all symptoms of infection. Any products collected in the 28 days before or the 14 days after resolution of symptoms should be recalled, quarantined and destroyed unless used for research.
    b. When a donor provides post donation information that he or she was the contact of a mumps case patient, as defined above, the donor should be deferred for 28 days after the last recognized contact. Any products collected from the first date of such contact until 28 days after the last recognized contact should be recalled, quarantined and destroyed, unless used for research.
6. Plasma for further manufacture (source and recovered) is not affected by these recommendations because virus inactivation procedures used to manufacture plasma derivatives should robustly inactivate this enveloped virus.

7. Collection facilities may want to consider refraining from the production and transfusion of fresh frozen plasma from collections from institutions or locales with epidemic mumps and diverting of such plasma for further manufacture. (Relabeling of previously manufactured fresh frozen plasma from such institutions or locales for further manufacture will require a variance from FDA as was required for West Nile virus in 2003.)
8. No recommendation is being made to perform consignee notification for the purpose of recipient notification at this time. However, some blood collection facilities, transfusion services and providers may wish to do so, to facilitate an estimate of the risk, if any, of transfusion transmission of the mumps virus. Appropriate samples for study might include plasma, serum and cells from the index donation for serology, viral culture and nucleic acid amplification, and the same on samples of recipients. Serial samples on the donor and recipients may be useful to study seroconversion and viral kinetics if infection is suspected.
9. Collection facilities that implement measures to prevent the theoretical transmission of mumps virus by transfusion should include notification to the FDA in their annual report.

America's Blood Centers (ABC) and American Red Cross (ARC) concur with these recommendations.

別紙様式第2-1

No. 22

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
				2006. 6. 20	該当なし	

一般的名称	(製造承認書に記載なし)	研究報告の公表状況	Fischer SA, Graham MB, Kuehnert MJ, Kotton CN, Srinivasan A, Marty FM, Comer JA, Guarner J, Paddock CD, DeMeo DL, Shieh WJ, Erickson BR, Bandy U, DeMaria A Jr, Davis JP, Delmonico FL, Pavlin B, Likos A, Vincent MJ, Sealy TK, Goldsmith CS, Jernigan DB, Rollin PE, Packard MM, Patel M, Rowland C, Helfand RF, Nichol ST, Fishman JA, Ksiazek T, Zaki SR; LCMV in Transplant Recipients Investigation Team. N Engl J Med. 2006 May 25;354(21):2235-49.	公表国
販売名(企業名)	合成血「日赤」(日本赤十字社) 照射合成血「日赤」(日本赤十字社)			米国

研究報告の概要

○臓器移植によるリンパ性脈絡髄膜炎ウイルス(LCMV)の伝播

背景:2003年12月及び2005年4月に固形臓器の移植を受けた2つの患者群を調査したところ、感染症を示唆する兆候と症状が発現した。診断によって得るものがなく、それぞれ共通のドナーが判明したため、各群に対する調査を実施した。

方法: 2名のドナー及び8名の被移植者から採取した試料を、ウイルス培養、電子顕微鏡、血清学的検査、分子解析、及び免疫組織化学染色により調べ、原因を明らかにした。臨床的経過の特徴を調査し、疾患の原因を特定するため、聞き取り調査、環境評価、カルテのレビューを含む疫学調査を実施した。

結果:検査により全ての被移植者にLCMVが認められたが、各集団に認められたのは、単一かつ独自の株であった。どちらの集団でも、LCMVはドナーから検出されなかった。2005年のドナーは、自宅で飼っていたペットのハムスターと接触しており、このハムスターは、被移植者で検出されたものと同一のLCMV株に感染していた。一方、2003年の集団ではLCMV感染源は認められなかった。被移植者は、移植後3週間以内に、腹痛、精神状態の変容、血小板減少症、トランスアミナーゼ値上昇、凝固障害、移植臓器の機能不全及び発熱又は白血球増多症を引き起こした。下痢、術創周囲の発疹、腎不全、及び痙攣の発現は一定しなかった。被移植者8名のうち7名が、移植後9から76日の間に死亡し、リバビリン投与及び減量した免疫抑制療法を受けていた被移植者1名が生存した。

結論: 臓器移植によるLCMV感染の伝播が見られた2つの集団についてまとめた。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「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

報告企業の意見	今後の対応
2003年12月及び2005年4月に固形臓器の移植を受けた2つの患者群でドナーからリンパ性脈絡髄膜炎ウイルスが伝播したと考えられたとの報告である。	今後も引き続き、新たなウイルス等による感染症の発生状況等に関する情報の収集に努める。

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of Lymphocytic Choriomeningitis Virus by Organ Transplantation

Staci A. Fischer, M.D., Mary Beth Graham, M.D., Matthew J. Kuehnert, M.D., Camille N. Kotton, M.D., Arjun Srinivasan, M.D., Francisco M. Marty, M.D., James A. Comer, Ph.D., Jeannette Guarner, M.D., Christopher D. Paddock, M.D., M.P.H.T.M., Dawn L. DeMeo, M.D., M.P.H., Wun-Ju Shieh, M.D., Ph.D., M.P.H., Bobbie R. Erickson, B.S., Utpala Bandy, M.D., M.P.H., Alfred DeMaria, Jr., M.D., Jeffrey P. Davis, M.D., Francis L. Delmonico, M.D., Boris Pavlin, M.D., Anna Likos, M.D., M.P.H., Martin J. Vincent, Ph.D., Tara K. Sealy, B.S., Cynthia S. Goldsmith, M.S., Daniel B. Jernigan, M.D., M.P.H., Pierre E. Rollin, M.D., Michelle M. Packard, M.P.H., Mitesh Patel, B.S., Courtney Rowland, B.S., Rita F. Helfand, M.D., Stuart T. Nichol, Ph.D., Jay A. Fishman, M.D., Thomas Ksiazek, D.V.M., Ph.D., Sherif R. Zaki, M.D., Ph.D., and the LCMV in Transplant Recipients Investigation Team*

ABSTRACT

BACKGROUND

In December 2003 and April 2005, signs and symptoms suggestive of infection developed in two groups of recipients of solid-organ transplants. Each cluster was investigated because diagnostic evaluations were unrevealing, and in each a common donor was recognized.

METHODS

We examined clinical specimens from the two donors and eight recipients, using viral culture, electron microscopy, serologic testing, molecular analysis, and histopathological examination with immunohistochemical staining to identify a cause. Epidemiologic investigations, including interviews, environmental assessments, and medical-record reviews, were performed to characterize clinical courses and to determine the cause of the illnesses.

RESULTS

Laboratory testing revealed lymphocytic choriomeningitis virus (LCMV) in all the recipients, with a single, unique strain of LCMV identified in each cluster. In both investigations, LCMV could not be detected in the organ donor. In the 2005 cluster, the donor had had contact in her home with a pet hamster infected with an LCMV strain identical to that detected in the organ recipients; no source of LCMV infection was found in the 2003 cluster. The transplant recipients had abdominal pain, altered mental status, thrombocytopenia, elevated aminotransferase levels, coagulopathy, graft dysfunction, and either fever or leukocytosis within three weeks after transplantation. Diarrhea, peri-incisional rash, renal failure, and seizures were variably present. Seven of the eight recipients died, 9 to 76 days after transplantation. One recipient, who received ribavirin and reduced levels of immunosuppressive therapy, survived.

CONCLUSIONS

We document two clusters of LCMV infection transmitted through organ transplantation.

From Rhode Island Hospital and Brown Medical School, Providence (S.A.F.); the Medical College of Wisconsin, Milwaukee (M.B.G.); the Divisions of Viral and Rickettsial Diseases (M.J.K., J.A.C., J.G., C.D.P., W.-J.S., B.R.E., B.P., A.L., M.J.V., T.K.S., C.S.G., P.E.R., M.M.P., M.P., C.R., R.F.H., S.T.N., T.K., S.R.Z.) and Healthcare Quality Promotion (A.S., D.B.J.), National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta; Massachusetts General Hospital and Harvard Medical School (C.N.K., F.L.D., J.A.F.) and Brigham and Women's Hospital and Harvard Medical School (F.M.M., D.L.D.) — all in Boston; the Rhode Island Department of Health, Providence (U.B.); the Massachusetts Department of Public Health, Boston (A.D.); the Wisconsin Department of Health and Family Services, Madison (J.P.D.); and the New England Organ Bank, Newton, Mass. (F.L.D.). Address reprint requests to Dr. Kuehnert at the Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., Mailstop A-30, Atlanta, GA 30333, or at mkuehnert@cdc.gov.

Drs. Ksiazek and Zaki contributed equally to this article.

*The members of the Lymphocytic Choriomeningitis Virus (LCMV) in Transplant Recipients Investigation Team are listed in the Appendix.

N Engl J Med 2006;354:2235-49.

LYMPHOCYTIC CHORIOMENINGITIS VIRUS (LCMV) is a rodent-borne, Old World arenavirus that has been reported to cause asymptomatic or mild, self-limited illness in otherwise healthy humans. It is a known cause of aseptic meningitis, but fatal infection is rare.[1-4] Transmission of infection from a woman to a fetus can result in hydrocephalus, chorioretinitis, or microcephaly.[5-8] Outside of vertical transmission during pregnancy, human-to-human transmission of LCMV has not been described.[9] We describe two clusters of unexplained clinical syndromes in transplant recipients and the subsequent investigations to identify donor-transmitted infection as the cause of illness.

METHODS

CASE REPORTS

The 2003 Cluster

In December 2003, unexplained febrile illnesses developed in four recipients of solid organs from a common donor (Fig. 1; additional information on clinical symptoms and laboratory findings for each recipient is listed in Table 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org).[10] Kidney Recipient 1 was a 46-year-old man with diabetes. Diarrhea and mild, diffuse abdominal pain developed on post-transplantation day 5, but his condition was stable and he was discharged home the following day. He was readmitted on post-transplantation day 23 with fever, persistent watery diarrhea, and worsening abdominal pain. Laboratory studies revealed leukopenia with elevated aminotransferase and creatinine levels. Ganciclovir therapy was initiated because of concern about possible cytomegalovirus infection. Tacrolimus and mycophenolate mofetil were discontinued. Examination of kidney-, liver-, and bone marrow–biopsy specimens did not reveal an infectious cause. On day 40 after transplantation, seizures and polymyoclonus developed. The patient reported blurred vision, and chorioretinitis was noted on ophthalmologic examination. Cerebrospinal fluid studies revealed a markedly elevated level of protein (720 mg per deciliter), a normal glucose level (147 mg per deciliter [8.2 mmol per liter]), and 4 white cells and 3 red cells per cubic centimeter. Polymerase-chain-reaction (PCR) tests for cytomegalovirus, herpes simplex virus, varicella–zoster virus, Epstein–Barr virus, human herpesvirus 6, enterovirus, adenovirus, *Mycobacterium tuberculosis*, and *Borrelia burgdorferi* were negative. Magnetic resonance imaging of the brain revealed bilateral, hemispheric, subdural fluid collections and diffuse dural thickening. Examination of a specimen obtained by dural biopsy on post-transplantation day 47 showed fibrosis; cidofovir and intravenous immune globulin were initiated for the suspected presence of an unknown viral pathogen. The patient's condition continued to deteriorate, and he died on post-transplantation day 53. An autopsy revealed bronchopneumonia and hepatic congestion without inflammation.

Figure 1 (facing page). Clinical Course of Lymphocytic Choriomeningitis Virus (LCMV) Infection in the 2003 Cluster.

MMF denotes mycophenolate mofetil, TMP-SMX trimethoprim–sulfamethoxazole, IVIG intravenous immune globulin, and X death. Immunosuppressive agents are shown in red, and antimicrobial agents in blue.

Kidney Recipient 2 was a 56-year-old man with glomerulonephritis. He was discharged home on post-transplantation day 5 but was readmitted on post-transplantation day 22 with fever, leukopenia, and peri-incisional erythema and tenderness. A skin-biopsy specimen obtained at the wound edge revealed basal-cell vacuolation suggestive of viral infection; no viral inclusions were seen, and immunohistochemical stains were negative for cytomegalovirus and adenovirus. Tacrolimus and mycophenolate mofetil were discontinued. Altered mental status and seizures with myoclonus developed on post-transplantation day 31. Cerebrospinal fluid studies revealed a markedly elevated protein level (620 mg per deciliter), a low glucose level (57 mg per deciliter [3.2 mmol per liter]), and 12 white cells (48 percent lymphocytes and 22 percent monocytes) and 6 red cells per cubic centimeter. PCR testing for the same infectious agents as in the case of Kidney Recipient 1 was unrevealing. Magnetic resonance imaging showed subdural fluid collections with diffuse dural enhancement. The patient's condition continued to deteriorate, with photophobia, nuchal rigidity, diarrhea, thrombocytopenia, diffuse erythroderma, respiratory failure, and atrial fibrillation, despite empirical administration of cidofovir and intravenous immune globulin. He died on post-transplantation day 76; an autopsy revealed meningoencephalitis and acute bronchopneumonia.