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DENGUE/DHF UPDATE 2009 (35)
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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>

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[1] Viet Nam
Date: Fri 29 Aug 2009
Source: Thanhnien News.com [edited]

Earlier this week, the Hanoi Health Department reported that nearly 2500 cases of the mosquito-borne illness had been recorded citywide since the beginning of the year [2009], 10 times more than over the same period last year [2008]. The department said the figures were the worst in years. "The number of dengue cases has gone up critically," said National Institute of Infectious and Tropical Diseases deputy director Nguyen Hong Ha, adding that the institute had admitted up to 45 dengue patients a day recently. "Around 100 patients are receiving treatment at the institute right now' we're on overload," he said. "Patients have to share beds, and we've even had to set up beds in the corridors. But that's still not enough; ... we're buying more beds."

According to the doctor, most of the patients had come from inner-city districts like Hoang Mai, Thanh Xuan, and Dong Da. He said that fact refuted the popular theory that the number of Hanoi dengue patients had gone up because the capital had absorbed parts of Hoa Binh and Vinh Phuc in 2008.

Although the number of dengue cases recorded in Ho Chi Minh City hasn't increased sharply this year [2009], more patients have reached critical condition, and there have been more deaths related to dengue, said Dr. Phan Van Nghiem from the city's health department. Over 7100 cases have been recorded citywide since the beginning of the year [2009], an increase of 5 percent compared with the same period last year [2008]. The city has already seen 7 deaths due to dengue, according to the department.

Doctor Le Bich Lien, head of the Dengue Fever Department at Children Hospital No. 1, said her facilities were treating around 80 kids for dengue, 1/4th of whom were in stages 3 and 4 with symptoms like circulatory failure, neurological problems and hemorrhaging. "Around 20-25 children are admitted to the hospital with dengue fever every day," said Dr. Lien. "HCMC kids account for 70 percent of our child patients."

Between 50 and 60 kids, mainly 3-10 years old, are receiving treatment

for dengue at HCMC Children Hospital No. 2, said Dr. Tran Thi Thuy, deputy head of the hospital's Infection Department. "Around 10 percent of them are in phase 4, the most critical phrase, and experiencing physical shock," Dr. Thuy said.

Thu Duc General Hospital has reported that some 20-30 dengue patients, mainly adults, were currently undergoing treatment there.

"During the 1st 1-2 days of infection, dengue in kids is difficult to distinguish from hand-foot-mouth disease or H1N1 flu," Lien said. "As H1N1 flu manifests itself in complicated ways, many people have let their guard down against dengue fever. But dengue can be fatal for kids," she warned.

[Byline: Thanh Tung-Lien Chau]

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Communicated by:
ProMED-mail Rapporteur Mary Marshall

A map of Viet Nam showing the provinces can be accessed at <http://www.lib.utexas.edu/maps/middle_east_and_asia/vietnam_admin01.jpg>. An interactive HealthMap/ProMED-mail of Viet Nam can be accessed at <http://healthmap.org/r/008c>. - Mod.TY]

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[2] Sri Lanka
Date: Sat 29 Aug 2009
Source: Xinhua News Agency [edited]
<http://news.xinhuanet.com/english/2009-08/29/content_11961338.htm>

The number of dengue cases has risen to 24 629 while 245 people have died of the disease in Sri Lanka so far this year [2009], the Epidemiological Unit of the Health Ministry said on Friday [28 Aug 2009].

The Epidemiological Unit said in its latest statistics that of the 24 629 cases, the highest number of patients were reported from June [2009] totaling 7048. It is followed by July [2009] with 6858 cases being reported.

This represents a sharp increase, as only 4156 dengue cases and 85 deaths were reported for the whole year of 2008.

Health officials said the majority of these cases have been reported from the areas of Kandy, Kegalle, Colombo, Gampaha and Kurunegala.

The rapid rise in the level of the epidemic has forced the health authorities to carry out extensive public awareness campaigns to eradicate the mosquito-based epidemic.

Households have been warned to keep the environment free of mosquitoes. Those who allow the mosquitoes to breed by allowing stagnating water face prosecution, with a special hotline being made available for public information.

There has been a decline in the number of dengue fever cases in August [2009], with 2387 cases being recorded as of [28 Aug 2009], officials said.

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Communicated by:
PRO/MBDS <promed-mbds@promedmail.org>

[During 2004 to 2009, the dengue outbreak in 2009 is the largest in Sri Lanka. Based on the above newswire, there have been 24 629 cases and 245 deaths so far (January-August 2009). The case fatality rate (CFR) is 0.99 percent. The number of reported dengue cases has dramatically increased nearly 6-fold as compared to 2008 (4156 cases).

At present, the trend of the dengue outbreak in Sri Lanka is decreasing, as there were 7048 cases, 6858 cases and 2378 cases reported in June, July and August 2009, respectively. However, more dengue outbreaks are also possible in November to February, when the

northeast monsoon begins.

Dengue is transmitted by the main vector, the _Aedes aegytpi_ mosquito. There are 4 distinct (but closely related) viruses that cause dengue. According to WHO's Regional Office for Southeast Asia (WHO/SEARO) report (available at <http://www.searo.who.int/en/Section10/Section332_1100.htm>), Sri Lanka, Indonesia, Thailand and Timor-Leste are classified in category A upon the transmission potential of dengue. The common characteristics among those countries are dengue fever (DF)/dengue haemorrhagic fever (DHF) as a major public health problem, which is the leading cause of hospitalization and death among children, and there are cyclical epidemics in urban centers and spreading to rural areas with multiple virus serotypes circulating.

In 2004, the total of dengue cases reported was 15 408 with 88 deaths (CFR 0.57) in Sri Lanka. During the past 20 years, the outbreak in 2004 was most serious, although the CFR was lower than in the past. Cases were reported every month, the highest being in June-July 2004. Cases were reported from 25 districts. Of these, 72 percent of cases and 78 deaths were from 5 cities, namely Colombo, Kandy, Gampaha, Kalutara and Kurunegala. The CFRs range from 0.4 percent to 1.1 percent.

In 2006, the reported dengue cases and deaths due to dengue had increased 2-fold as compared to 2005. The case fatality was maintained below one percent. In 2007 till May, 1846 dengue cases and 9 deaths have been reported from Sri Lanka (see <http://www.searo.who.int/en/Section10/Section332/Section2277_11963.htm>).

A map of Sri Lanka can be accessed at <http://www.lib.utexas.edu/maps/middle_east_and_asia/sri_lanka_pol01.jpg>. A HealthMap/ProMED-mail interactive map of Sri Lanka can be accessed at <http://healthmap.org/r/009M>. - Mod.SCM]

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[3] Myanmar (Rakhine)
Date: Mon 24 Aug 2009
Source: Mizzima News [edited]
<http://www.mizzima.com/news/inside-burma/2666-dengue-kills-three-afflicts-over

According to information from the Ministry of Health, at least 3 people have died and 329 have been infected with dengue fever this year [2009] in Sittwe and Kyaukphyu of Arakan [Rakhine] State in western Burma [Myanmar].

According to the ministry of health, 2 people in Sittwe, capital of Arakan [Rakhine] state, have died and another in Kyaukphyu town.

"Though dengue is not very dangerous, 2 people died in our town, scaring people. There are many dengue afflicted child patients in hospital, but I cannot tell the exact number. Besides, there are many more unreported cases in the villages. The villagers cannot afford treatment at the hospital. Only the affluent in the town can get admitted to the hospital. Dengue has infected not only children but adults as well. There are many people from different age groups being treated at our hospital. Most patients are children, and the fever lasts less than a week, after which the patient is out of danger," a doctor in Sittwe Hospital said.

But some patients need to be treated for over a week. "My daughter had dengue since the beginning of this month [August 2009] and was hospitalized as soon as she was infected. Now she has been discharged. Though her condition has improved, she has not yet fully recovered. She has been absent from school for over 2 weeks," [her mother] in Sittwe told Mizzima.

Teachers are worried about their students, as many are absent from schools. "There are many children who cannot come to school because of the flu. Their friends say they either have flu or dengue fever. Some could not come to school for a whole month [August 2009]. We are worried about their education given the long absence from classes," a class teacher in the State High School No. 2 in Sittwe told Mizzima.

Though the symptoms of this disease are coughing, sneezing, fever, and

body ache, in this type of influenza, similar symptoms are not found, and there are only sudden high fever plus headaches.

Rash, bleeding from the nose and gums, bloodstains in the urine and stool were found in these patients. Patients are known to become unconscious, have convulsions, perspire with high fever, vomit continuously, and suffer from shock.

Dengue fever cases were also reported in Pyi, Pa-an in Karen State and Htantalan town in Chin State.

The Health Ministry release said that about 30 people die of dengue fever in Rangoon [Yangon] annually.

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Communicated by:
PRO/MBDS <promed-mbds@promedmail.org>

[The newswire above is the 4th report of dengue cases and deaths in Myanmar since mid June 2009. However, it is the 1st report from Rakhine state (formerly Arakan), one of 7 states of Myanmar situated along the western coast. According to the newswire, there have been 329 dengue fever cases with 3 fatalities (2 cases from Sittwe and another one from Kyaukphyu town) during 2009.

The previously reported dengue outbreak in Myanmar occurred in Myitkyina, capital of Kachin State (see prior PRO/MBDS posting Dengue Myanmar (03): RFI 20090728.2650). There are no current reports of morbidity and mortality statistics in the country with respect to dengue fever in 2009. However, as of 24 Jul 2009, there were 838 cases with 6 deaths of dengue during 2009 in Yangon, Myanmar (see prior PRO/MBDS posting Dengue - Myanmar (02): Yangon 20090726.2635).

In Myanmar, dengue fever (DF)/dengue haemorrhagic fever (DHF) is one of the leading causes of morbidity and mortality among children under the age of 10 years, with approximately 85 percent of cases occurring in this age group. An annual average of 7000-10 000 cases of DF/DHF are reported nationwide. However, in recent epidemic years (2001, 2005, and 2007), the number had risen to over 15 000 cases. In 2007, 62 percent of all reported cases were from Yangon Division (31 percent), Ayeyarwaddy Division (16 percent) and Mon State (15 percent) (1).

The 1st major epidemic of the disease syndrome in Myanmar occurred in the capital, Yangon in 1970. Since then, epidemics have continued to occur in a cyclic pattern, and the disease has spread from Yangon to most parts of the country. Between 1970 and 1995, there were 83 381 cases of DHF with 3243 deaths, a case fatality rate of 3.88 percent. During the 1st 5 years in which DHF was known to occur in the country, almost all the cases were confined to the Yangon division. By 1975, the disease syndrome had begun to spread and, in that year, 31 percent of the DHF cases occurred in Mandalay and only 29 percent in Yangon. However, Yangon still remains the most serious focus of DHF (2).

According to WHO's Regional Office for South-East Asia (WHO/SEARO) report available at <http://www.searo.who.int/EN/Section10/Section332/Section2277_11962.htm>, in 2005 the total dengue cases reported was 17 454 and 169 deaths in Myanmar, and the case fatality rate was maintained below one percent. The increase in case load and deaths compared to 2004 is almost 2 times. In 2006, the reported dengue cases and deaths were reduced as compared to 2005. The case fatality rate in 2006 was slightly above one percent. The seasonal trend shows July as the peak month, and cases start increasing from May to peak in July-August.

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2. Prasittisuk C, Andjaparidze AG, Kumar V. WHO South-East Asia Regional Office: Current Status of Dengue/Dengue Haemorrhagic Fever in WHO South-East Asia Region. Dengue Bulletin Volume 22, December 1998 (available at

<http://www.searo.who.int/en/Section10/Section332/Section520_2414.htm>).

For maps of Myanmar see
<http://www.worldatlas.com/webimage/countrys/asia/lgcolor/mmcolor.htm>
and
<http://www.lib.utexas.edu/maps/middle_east_and_asia/burma_pol_96.jpg>. For the interactive HealthMap/ProMED-mail map of Myanmar with links to other ProMED-mail reports in Myanmar and surrounding countries, see <http://healthmap.org/r/00IU>. - Mod.SCM]

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[4] India (Gujarat)
Date: Mon 31 Aug 2009
Source: Times of India [edited]
<http://timesofindia.indiatimes.com/NEWS/City/Rajkot/Dengue-outbreak-gets-sever

The dengue outbreak in the city is refusing to die down, with 15 cases reported in the city in the past 48 hours. With 3 fresh cases reported on Sunday [30 Aug 2009], the total number of patients being treated for the disease in the city has gone up to 55. One person has died of the disease till date. The patients were admitted from Sukhnathpara, Sardarnagar and Baharwadi areas. On Saturday [29 Aug 2009], there were 7 new cases reported.

"We are doing our best to tackle the situation in the city. The district collector PR Sompura has formed a special team to root out the virus from the city. Daily, 10 teams under this special team are conducting door-to-door surveys along with officials from Amreli municipality, to find out cases," a district health official said.

Apart from health officials, teams from the municipality are also conducting cleanliness drives throughout the city. "We are fumigating all streets of the city every evening to kill mosquitoes carrying the dengue virus and cleaning any water-logged areas. However, our job will get more challenging with the 2nd spell of rainfall that has begun since the past 72 hours," an official from Amreli Nagar Palika said.

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[Fumigating the streets will be of only temporary value. Eliminating the vector mosquito breeding sites in and around houses and other buildings will provide more effective control of the outbreak.

An interactive map of Gujarat, India showing the location of Amreli and vicinity can be accessed at
<http://www.maplandia.com/india/gujarat/amreli/amreli/>. A HealthMap/ProMED-mail interactive map of India can be accessed at <http://healthmap.org/promed/en?v=22.9,79.6,5>. - Mod.TY]

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[5] Pakistan
Date: Wed 26 Aug 2009
Source: The News [edited]
<http://www.thenews.com.pk/print1.asp?id=195030>

Out of 18 patients of a locality admitted to Holy Family Hospital Saturday [22 Aug 2009] evening, 5 were declared positive for dengue fever by the National Institute of Health (NIH), Islamabad. The confirmation of 5 cases as positive, the 1st in this season in this region of the country, has convinced a number of health experts in town to fear an outbreak of the infection.

"The confirmation of 5 cases proved the existence of _Aedes aegypti_, the female mosquito that causes dengue fever [transmits dengue viruses] in town. The deaths of 2 children on Friday night and Saturday morning [21 and 22 Aug 2009] due to fever in the area from where 18 patients have been taken might be attributed to dengue fever or DHF," said NIH.

A special team of the District Health Department headed by District Health Officer Dr. Khalid Randhawa has shifted some 16 children and 2 adults to the HFH after suspecting them cases of dengue fever on Saturday evening [29 Aug 2009] from a village not more than 25 km from here. The team was constituted after the Executive District Officer (Health) received reports of deaths of the 2 children. The deceased as well as all the suspects admitted at HFH have been living in a cluster of nearly a dozen families settled near the village Larr in Dhoke Jhando, located in union council Thatta Khalil of Taxila.

All the 5 cases confirmed so far for the infection range between 3 and 8 years of age. The HFH has sent blood samples of a total of 18 suspected patients of dengue fever to NIH for dengue serology, of which 5 have been confirmed positive, 9 negative, while results of 4 cases have not been finalised as yet.

Experts do believe that with the detection of 5 confirmed cases in the outskirts of twin cities of Islamabad and Rawalpindi, a rising threat of an outbreak of dengue and DHF seems to be lurking, as the disease has a tendency to occur in epidemics and outbreaks and spreads like wild fire.

Head of Pathology Department at Rawalpindi Medical College Professor Dr. Abbas Hayat has repeatedly expressed to "The News" that the spikes of dengue fever, if they occur repeatedly, might be more deadly and might result in severe complications, including hemorrhagic manifestations. Two months back, he said that the situation might be alarming after the monsoon, as the climate after monsoon is considered to be the most suitable for the breeding of the mosquito _Aedes aegypti_ that causes [transmits the viruses that cause] DF and DHF. DHF is a cause of disease and death primarily among children in tropical Asia.

Studies have revealed that people at a higher risk for dengue transmission are children, travellers and tourists, whereas adults residing in endemic areas are also susceptible to contracting the disease.

The District Health Department has already claimed that it has performed fogging and sprinkled insecticidal spray in and around Larr; however, experts believe that a continuous surveillance is needed at this time to avert a possible outbreak of dengue fever.

[Byline: Muhammad Qasim]

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Communicated by:
HealthMap Alerts via
ProMED-mail <promed@promedmail.org>

[A HealthMap/ProMED-mail interactive map of Pakistan can be accessed at <http://healthmap.org/promed/en?v=30,69.4,5>. - Mod.TY]

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[6] Mauritius
Date: Thu 17 Aug 2009
Source: Eurosurveillance [edited]
<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19314>

[The following article presents an interesting approach for mapping dengue outbreaks. - Mod.TY]

Abstract
During the month of June 2009, Mauritius experienced a short-lived outbreak of dengue fever localised in its capital city Port Louis. _Aedes albopictus_, a secondary vector of dengue viruses, was the probable vector. We introduce a method which combines Google Earth images, stochastic cellular automata and scale free network ideas to map this outbreak. The method could complement other techniques to forecast the evolution of potential localised mosquito-borne viral outbreaks in Mauritius and in at-risk locations elsewhere for public health planning purposes.

Reference;

Ramchurn SK, Moheeput K, Goorah SS. 2009. An analysis of a short-lived outbreak of dengue fever in Mauritius. Euro Surveill 14:19314. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19314>.

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[A HealthMap/ProMED-mail interactive map of Mauritius can be accessed at: <http://healthmap.org/promed/en?v=-20.3,57.9,5>. - Mod.TY]

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[7] Dominican Republic
Date: Fri 28 Aug 2009
Source: El Nuevo Diario [in Spanish, trans. Mod.TY, edited]
<http://elnuevodiario.com.do/app/article.aspx?id=165814>

A dozen people, including adults and children, are affected by dengue, with one of these in a serious state, reported the representative of the municipal district Canca La Reina, Licenciado Manuel Antonio Rojas. The district executive said that the dreaded dengue outbreak that hit the different communities of Canca la Reina is produced by a strong wave of mosquitoes left by the passage of recent rains that have fallen in the past weeks. He recalled that in 2003, 4 people died in this community, affected by dengue, which is the reason that a call was issued to the provincial Health Directorate so that urgent measures would be taken together with the municipal government to avoid a repetition of that history. Tony Rojas said that the municipal government has maintained operations to eradicate trash, mosquito breeding sites and wells where the mosquito that is the dengue vector breeds.

He pointed out that the outbreak has become present in various communities of Canca La Reina, but the main effects have occurred in the Manhattan sector, where there is an affected child in an extremely serious state. "We have called Public Health on other occasions to carry out work against the dengue vector mosquito, but they have not reciprocated," complained Representative Tony Rojas. He said that the situation is very serious because there are more than 12 people affected by dengue.

Representative Tony Rojas stated that the municipal government is coordinating an urgent operation to tackle the epidemic of mosquitoes, stressing that the health of the population of Canca La Raina is in danger.

[Byline: Arcadio B. Rojas]

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Communicated by:
HealthMap Alerts via
ProMED-mail <promed@promedmail.org>

[A HealthMap/ProMED-mail interactive map showing the Dominican Republic and its location in the Caribbean can be accessed at <http://healthmap.org/promed/en?v=18.9,-70.5,5>. - Mod.TY]

[see also:
Dengue/DHF update 2009 (34) 20090823.2977
Dengue/DHF update 2009 (33) 20090817.2908
Dengue/DHF update 2009 (32) 20090811.2864
Dengue/DHF update 2009 (31) 20090803.2723
Dengue/DHF update 2009 (29) 20090720.2574
Dengue/DHF update 2009 (28) 20090713.2501
Dengue/DHF update 2009 (27) 20090706.2425
Dengue/DHF update 2009 (26) 20090629.2353
Dengue/DHF update 2009 (25) 20090622.2286
Dengue/DHF update 2009 (24) 20090614.2211
Dengue/DHF update 2009 (23) 20090608.2121
Dengue/DHF update 2009 (22) 20090601.2040
Dengue/DHF update 2009 (21) 20090525.1952
Dengue/DHF update 2009 (20) 20090518.1868
Dengue/DHF update 2009 (19) 20090512.1774

Dengue/DHF update 2009 (18) 20090505.1677
Dengue/DHF update 2009 (17) 20090428.1595
Dengue/DHF update 2009 (16) 20090419.1485
Dengue/DHF update 2009 (14) 20090406.1341
Dengue/DHF update 2009 (13) 20090331.1227
Dengue/DHF update 2009 (12) 20090314.1049
Dengue/DHF update 2009 (08) 20090216.0650
Dengue/DHF update 2009 (06) 20090210.0603]
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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
				2009. 9. 16	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		
			Aguilar PV, Camargo W, Vargas J, Guevara C, Roca Y, Felices V, Laguna-Torres VA, Tesh R, Ksiazek TG, Kochel TJ. Emerg Infect Dis. 2009 Sep;15(9):1526-8.	公表国 ボリビア
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)			

研究報告の概要	使用上の注意記載状況・その他参考事項等
○ボリビア出血熱の再興(2007～2008年) ボリビア出血熱(BHF)は、1959年に、ボリビア東部でのアウトブレイク発生時に初めて報告された。しかし、病原体のマチュポウイルスが死亡患者の脾臓から分離されたのは、1963年であった。1976～1993年は症例が報告されなかったが、1994年にアウトブレイクが起こり、以降、散発症例が観察されていた。 2007年の2月、3月に、BHF疑い症例20例以上(死亡3例)がボリビア北東部ベニの保健当局(SEDES)に報告されていた。2008年2月には、疑い症例200例以上(死亡12例)がSEDESに報告された。 疑い例患者から採取した血清19検体について、間接免疫蛍光法とPCRで検査を行った。アレナウイルスの分離株が5株得られ、遺伝子配列の解析からマチュポウイルスであることが確認された。	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

報告企業の意見	今後の対応
2007年の2月、3月に、ボリビア出血熱の疑い症例20例以上、2008年2月には200例以上が報告され、19例について検査したところ、5例でマチュポウイルスが確認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。また、発熱などの体調不良者を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。

Table. Characteristics *Mycobacterium bovis* BCG complication cases, Taiwan, 2005–2007*

Patient no.	Sex/age at diagnosis, y	Year reported	Specimen	Diagnosis and site of involvement
1	F/2	2005	Biopsy sample	BCG osteitis/osteomyelitis, right ankle
2	M/1	2005	Bacterial isolate	Subcutaneous abscess, left anterior chest wall
3	M/2	2005	Bacterial isolate	Severe combined immunodeficiency, disseminated BCGitis
4	M/9	2005	Bacterial isolate	Suppurative lymphadenitis
5	F/1	2005	Bacterial isolate	Injection-site abscess
6	M/1	2005	Biopsy sample	Suppurative lymphadenitis
7	M/2	2006	Bacterial isolate	BCG osteitis/osteomyelitis, right distal femoris
8	M/2	2006	Bacterial isolate	BCG osteitis/osteomyelitis
9	F/1	2006	Bacterial isolate	BCG osteitis/osteomyelitis, left distal femoris
10	F/1	2006	Bacterial isolate	BCG osteitis/osteomyelitis, left distal radius
11	F/2	2007	Bacterial isolate	BCG osteitis/osteomyelitis, right knee
12	M/1	2007	Bacterial isolate	Subcutaneous abscess, left wrist
13	M/2	2007	Biopsy sample	BCG osteitis/osteomyelitis, right ankle
14	F/1	2007	Bacterial isolate	Suppurative lymphadenitis
15	M/2	2007	Bacterial isolate	BCG osteitis/osteomyelitis, left proximal tibia

*BCGitis, disseminated BCG infection.

age. In particular, suspected childhood TB patients without an identifiable TB contact and with normal immune status were subjected to further investigations. Multidisciplinary management, including enhanced laboratory diagnosis of atypical bony lesions in infants and children, is recommended for any suspected TB infection. Once BCG-related infection is confirmed, medical treatment has to be consistent.

Acknowledgments

We thank Steve H. S. Kuo, Toru Mori, and Jen Suo for comments and Chen-Che Chiu and Chien-Chung Huang for excellent technical assistance.

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Ruwen Jou, Wei-Lun Huang, and Wei-Ju Su

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Reemergence of Bolivian Hemorrhagic Fever, 2007–2008

To the Editor: Bolivian hemorrhagic fever (BHF) was first described in 1959 during outbreaks affecting isolated human communities in eastern Bolivia. However, it was not until 1963 that the etiologic agent, Machupo virus, was isolated from the spleen of a patient who died from this disease (*1*). Although no cases were reported between 1976 and 1993, an outbreak occurred in 1994 and sporadic cases have been observed since then.

In February and March 2007, at least 20 suspected BHF cases (3 fatal) were reported to the El Servicio Departamental de Salud (SEDES) in Beni,

Bolivia. In February 2007, physicians at the Hospital Santa Maria Magdalena reported 3 male patients (23, 27, and 29 years of age), who worked at a ranch in Magdalena, Itenez Province (13°14′0″S, 64°12′0″W). The patients sought treatment for fever, gingivorrhagia, petechiae, nausea, hematemesis, melena and tremors; clinical laboratory examinations showed thrombocytopenia (<130,000 cells/mm^3), leukopenia (<3,900 cells/mm^3), and hematuria. Because physicians suspected BHF, patients received supportive therapy, including intravenous hydration, corticoids, antipyretic drugs, antimicrobial drugs, and blood transfusions from donors who had survived Machupo virus infection. Nonetheless, 2 of the patients died 3 and 4 days after admission.

In February 2008, at least 200 suspected new BHF cases (12 fatal) of BHF were reported to SEDES. A febrile hemorrhagic illness developed in a 19-year-old man from Huacaraje, Itenez Province (13°33′S, 63°45′W). On first examination at the Hospital Santa Maria Magdalena, the patient had fever, tremor, gingivorrhagia, petechiae, bruises, asthenia, and anorexia and was admitted with a presumptive diagnosis of BHF. Despite supportive treatment (including administration of plasma from a BHF survivor), his condition worsened; hematemesis, melena, hematochezia, hematuria, anuria, respiratory alkalosis, and metabolic acidosis developed in the patient, eventually resulting in death. A fifth case was detected in a 46-year-old man from San Ramon, Mamore Province (13°17′0″S, 64°43′0″W). A febrile hemorrhagic illness developed in the patient and he was admitted to the Hospital German Busch in Trinidad. The patient recently had been hired as a farm worker. When first seen by the attending physicians, he had fever, thrombocytopenia, leukopenia, petechias, tremors, gingivorrhagia, and dehydration, consistent with symptoms of BHF. The patient received hydration, corticoids, antipyretic therapy, and a plasma transfusion from a BHF survivor. The patient's condition improved and he was subsequently discharged from the hospital ≈10 days after admission.

Nineteen serum samples collected from suspected BHF patients, including the cases described above, were sent to Centro Nacional de Enfermedades Tropicales (Santa Cruz, Bolivia) and the US Naval Medical Research Center Detachment (Lima, Peru) for testing. Serum was injected into Vero and C6/36 cells; 10 days later, the cells were tested for flaviviruses, alphaviruses, and arenaviruses by indirect immunofluorescent assay and PCR. Five arenavirus isolates were obtained from the patients described in this report.

Viral RNA was extracted from the cell culture supernatant and the small (S) segment (≈3,200 bp) was amplified and sequenced. Phylogenetic analyses were conducted using the neighbor-joining and maximum likelihood program implemented in PAUP 4.0 software (Sinauer Associates, Inc., Sunderland, MA, USA). Sequence analyses confirmed the isolates as Machupo virus (Figure). Eight major Machupo phylogenetic lineages were described based on partial sequence of the nucleocapsid protein gene (*2*). We observed a similar tree topology based on the glycoprotein gene sequences (Figure). Two distinct lineages were distinguished among the isolates from the Itenez and Mamore provinces: V and VII and I and II, respectively. The recent isolates (2007–2008) from Magdalena and Huacaraje (Itenez Province) grouped within lineage V whereas the 2008 isolate from San

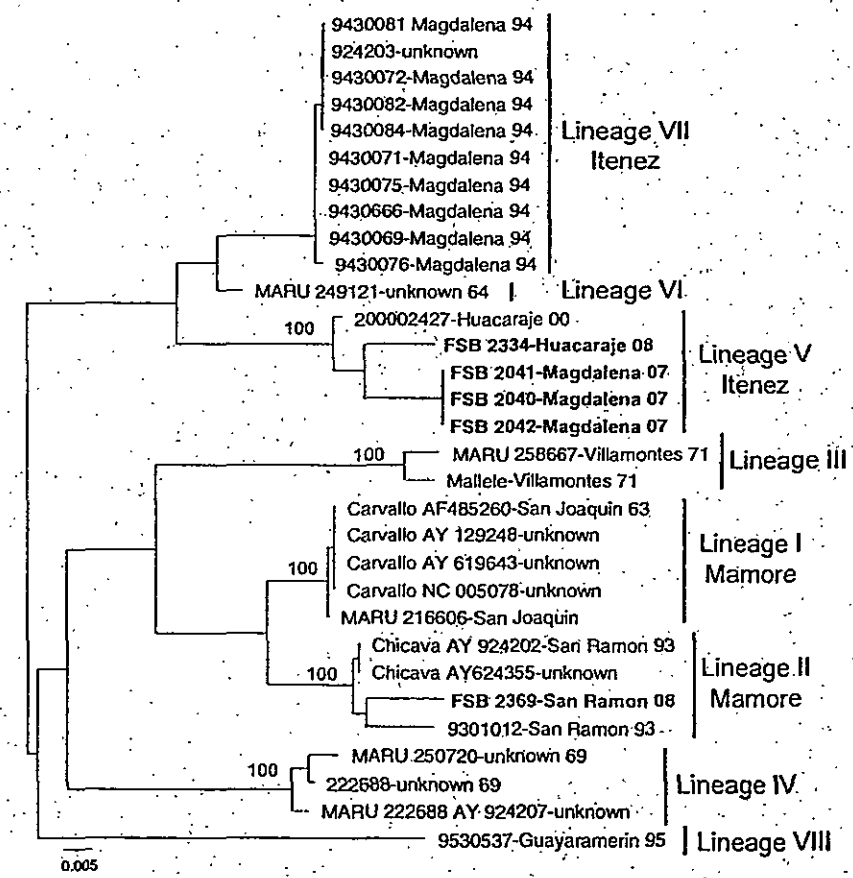

Figure. Neighbor-joining phylogenetic tree of Machupo virus derived from the glycoprotein precursor gene sequence. The neighbor-joining and maximum likelihood analyses yielded similar phylogenetic trees. Boldface indicates 2007–2008 isolates. Numbers indicate bootstrap values for 1,000 replicates. Scale bar indicates nucleotide substitutions per site.

Ramon (Mamore Province) belonged to lineage II. These isolates showed 10% nucleotide difference within the S segment and a 6% amino acid difference within the glycoprotein precursor gene. Similar genetic diversity has been described with Machupo virus and other arenaviruses (*2–4*). Sequences generated were deposited in GenBank (accession nos. FJ696411, FJ696412, FJ696413, FJ696414, and FJ696415).

It is not known whether lineage VII and I viruses continue to circulate or have been replaced by lineage V and II viruses, respectively. This study confirms the long-term maintenance of distinct phylogenetically forms of Machupo virus in a small area within Beni. Although the distribution of the Machupo virus rodent reservoir (*Calomys callosus*) extends beyond the geographic area of the Machupo cases described, factors that limit the endemic distribution of the virus remain unknown. However, population differences among *C. callosus* may account for the natural nidality of BHF (*5*). Studies are needed to fully identify and understand the ecology of the rodent reservoir and Machupo virus transmission.

Machupo virus continues to cause sporadic cases and focal outbreaks of BHF in Bolivia. We describe 5 confirmed human cases (3 fatal) of Machupo virus infection in Beni Department, Bolivia, an area in which BHF is endemic. That all 5 patients were farmers suggests their infections were probably acquired through occupational exposure. Although all the patients received plasma transfusion from patients who had survived BHF infection, 3 patients still died. An early diagnosis and the rapid administration of Machupo immune plasma before the hemorrhagic phase may increase the chance of survival, as has been observed with other arenavirus infections (*6–8*).

Acknowledgments

We thank Roxana Caceda and Juan Sulca for excellent technical assistance and the personnel of the Bolivian Ministry of Health for supporting our febrile illness surveillance study. Local activities were approved by the Ministry of Health of Bolivia and were developed by CENETROP personnel through local coordinators.

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Relapsing Fever Spirochete in Seabird Tick, Japan

To the Editor: Tick-borne relapsing fever (TBRF) is caused by infection with spirochetes belonging to the genus *Borrelia*. We previously reported a human case of febrile illness suspected to be TBRF on the basis of serologic examination results; the vector most likely was a genus *Carios* tick that had fed on a seabird colony (*1*). However, surveillance of ticks in the area did not identify *Borrelia* spp. in any of the *Carios* ticks sampled (2). In 2007 and 2008, a borreliosis investigation was conducted on Kutsujima Island (35.71′N, 135.44′E) because

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研究報告の概要

○慢性疲労症候群患者の血液細胞における感染性レトロウイルスXMRVの検出
慢性疲労症候群(CFS)は原因不明の疾患で、全世界に1700万人の患者がいると推定されている。CFS患者の末梢血単核細胞(PBMCs)を検討することにより、患者101名中68名(67%)、健常者の対照群218名中8名(3.7%)において、ヒトガンマレトロウイルスの一種であるxenotropic murine leukemia virus-related virus(XMRV)のDNAを同定した。細胞培養試験では、患者由来XMRVに感染性があり、細胞結合性感染、無細胞性感染のいずれも起こりうることが判明した。CFS患者由来の活性化PBMCs、B細胞、T細胞、血漿への暴露後に、非感染初代リンパ球と指標細胞株において二次感染が成立した。これらの知見はXMRVがCFSの病原因子である可能性を提起する。

報告企業の意見	今後の対応
慢性疲労症候群(CFS)患者の血液細胞から感染性レトロウイルスXMRVのDNAが検出され、XMRVがCFSの病原因子である可能性が提起さ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

赤血球濃厚液-LR「日赤」
照射赤血球濃厚液-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

the pathophysiology of chytridiomycosis appears to be disruption to the osmoregulatory functioning of the skin and consequent osmotic imbalance that leads to cardiac standstill.

To test whether treating electrolyte abnormalities would reduce the clinical signs of disease, we administered an oral electrolyte supplement to *L. caerulea* in the terminal stages of infection, when they lost the righting reflex and could no longer correct their body positions (*26*). Frogs under treatment recovered a normal posture and became more active; one individual recovered sufficiently to climb out of the water onto the container walls, and two individuals were able to jump to avoid capture. These signs of recovery were not observed in any untreated frogs. In addition, treated frogs lived >20 hours longer than untreated frogs [mean time after treatment ± SEM: treated frogs (N = 9), 32 ± 2.8 hours; control frogs (N = 6), 10.7 ± 2.2 hours; Student's t test, $P < 0.001$]. All treated frogs continued to shed skin and ultimately died from the infection, as expected. It is unlikely that electrolyte treatment could prevent death unless the epidermal damage caused by *Bd* is reversed. Although amphibians can generally tolerate greater electrolyte fluctuations than other terrestrial vertebrates (*18*), we suggest that depletion of electrolytes, especially potassium, is important in the pathophysiology of chytridiomycosis. Amphibian plasma potassium concentrations are maintained at constant levels across seasons (*27*), and even moderate hypokalemia is dangerous in humans (*28*).

Our results support the epidermal dysfunction hypothesis, which suggests that *Bd* disrupts cutaneous osmoregulatory function, leading to electrolyte imbalance and death. The ability of *Bd* to compromise the epidermis explains how a superficial skin fungus can be fatal to many species of amphibians; their existence depends on the physiological interactions of the skin with the external environment (*16*–*19*). Disease outbreaks capable of causing population declines require the alignment of multiple variables, including a life-compromising pathophysiology (*1*). Resolving the pathogenesis of chytridiomycosis is a key step in understanding this unparalleled pandemic.

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Supporting Online Material

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Materials and Methods
SOM Text
Figs. S1 and S2
Tables S1 and S2
References

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Detection of an Infectious Retrovirus, XMRV, in Blood Cells of Patients with Chronic Fatigue Syndrome

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Chronic fatigue syndrome (CFS) is a debilitating disease of unknown etiology that is estimated to affect 17 million people worldwide. Studying peripheral blood mononuclear cells (PBMCs) from CFS patients, we identified DNA from a human gammaretrovirus, xenotropic murine leukemia virus–related virus (XMRV), in 68 of 101 patients (67%) as compared to 8 of 218 (3.7%) healthy controls. Cell culture experiments revealed that patient-derived XMRV is infectious and that both cell-associated and cell-free transmission of the virus are possible. Secondary viral infections were established in uninfected primary lymphocytes and indicator cell lines after their exposure to activated PBMCs, B cells, T cells, or plasma derived from CFS patients. These findings raise the possibility that XMRV may be a contributing factor in the pathogenesis of CFS.

Chronic fatigue syndrome (CFS) is a disorder of unknown etiology that affects multiple organ systems in the body. Patients with CFS display abnormalities in immune system function, often including chronic activation of the innate immune system and a deficiency in natural killer cell activity (*1*, *2*). A number of viruses, including ubiquitous herpesviruses and enteroviruses, have been implicated as possible environmental triggers of CFS (*1*). Patients with CFS often have active β herpesvirus infections, suggesting an underlying immune deficiency.

The recent discovery of a gammaretrovirus, xenotropic murine leukemia virus–related virus (XMRV), in the tumor tissue of a subset of prostate cancer patients prompted us to test whether XMRV might be associated with CFS. Both of these disorders, XMRV-positive prostate cancer and CFS, have been linked to alterations in the antiviral enzyme RNase L (*3*–*5*). Using the Whittemore Peterson Institute's (WPI's) national

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tissue repository, which contains samples from well-characterized cohorts of CFS patients, we isolated nucleic acids from PBMCs and assayed the samples for XMRV *gag* sequences by nested polymerase chain reaction (PCR) (*5*, *6*). Of the 101 CFS samples analyzed, 68 (67%) contained XMRV *gag* sequence. Detection of XMRV was confirmed in 7 of 11 WPI CFS samples at the Cleveland Clinic by PCR-amplifying and sequencing segments of XMRV *env* [352 nucleotides (nt)] and *gag* (736 nt) in CFS PBMC DNA (Fig. 1A) (*6*). In contrast, XMRV *gag* sequences were detected in 8 of 218 (3.7%) PBMC DNA specimens from healthy individuals. Of the 11 healthy control DNA samples analyzed by PCR for both *env* and *gag*, only one sample was positive for *gag* and none for *env* (Fig. 1B). In all positive cases, the XMRV *gag* and *env* sequences were more than 99% similar to those previously reported for prostate tumor–associated strains of XMRV (VP62, VP35, and VP42) (fig. S1) (*5*).

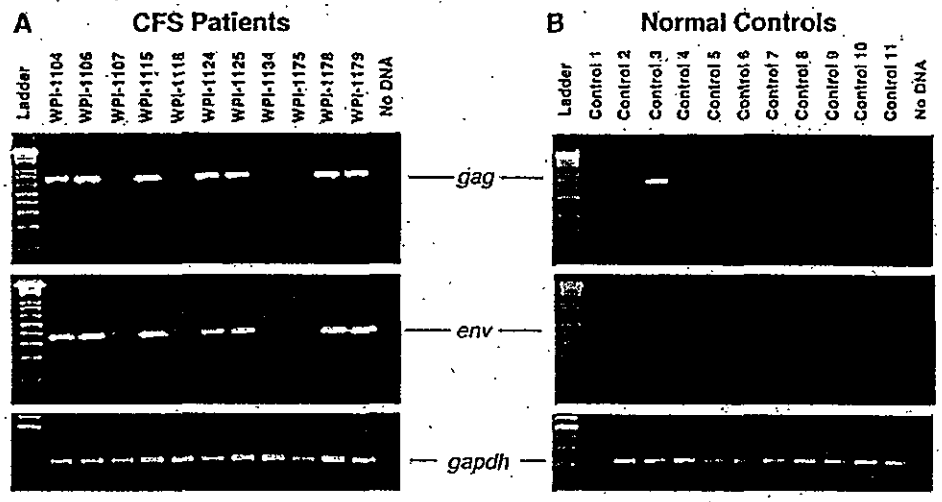

Fig. 1. XMRV sequences in PBMC DNA from CFS patients. Single-round PCR results for *gag*, *env*, and *gapdh* sequences in PBMCs of (**A**) CFS patients and (**B**) healthy controls are shown. The positions of the amplicons are indicated and DNA markers (ladder) are shown. These are representative results from one group of 20 patients.

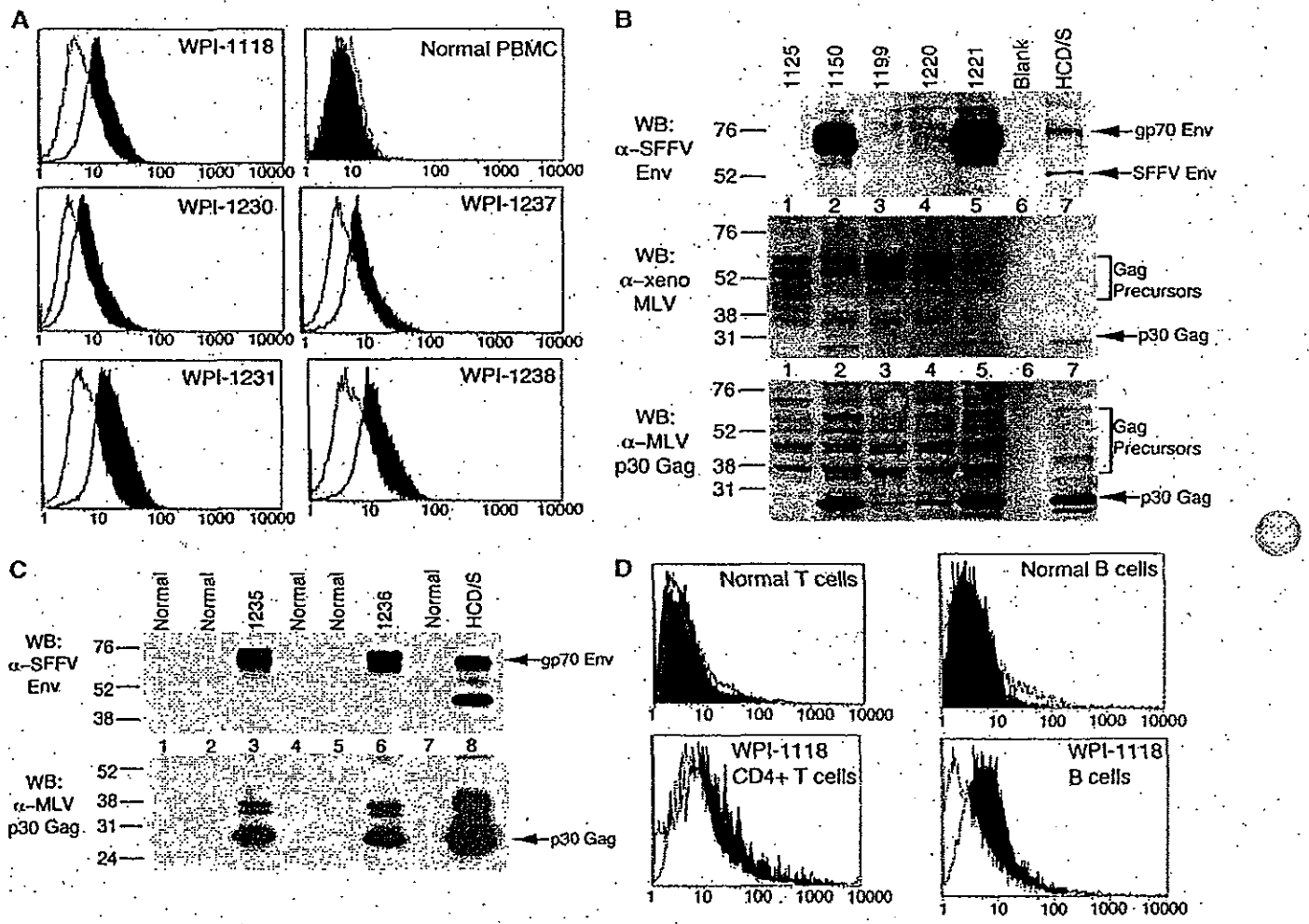

Fig. 2. Expression of XMRV proteins in PBMCs from CFS patients. (**A**) PBMCs were activated with phytohemagglutinin and interleukin-2, reacted with a mAb to MLV p30 Gag, and analyzed by IFC. (**B**) Lysates of activated PBMCs from CFS patients (lanes 1 to 5) were analyzed by Western blots with rat mAb to SFFV Env (top panel), goat antiserum to xenotropic MLV (middle panel), or goat antiserum to MLV p30 Gag (bottom panel). Lane 7, lysate from SFFV-infected HCD-57 cells. Molecular weight markers in kilodaltons are at left. (**C**) Lysates of activated PBMCs from healthy donors (lanes 1, 2, 4, 5, and 7) or from CFS patients (lanes 3 and 6) were analyzed by Western blots using rat mAb to SFFV Env (top panel) or goat antiserum to MLV p30 Gag (bottom panel). Lane 8, SFFV-infected HCD-57 cells. Molecular weight (MW) markers in kilodaltons are at left. (**D**) $CD4^+$ T cells (left) or $CD19^+$ B cells (right) were purified, activated, and examined by flow cytometry for XMRV Gag with a mAb to MLV p30 Gag.

Sequences of full-length XMRV genomes from two CFS patients and a partial genome from a third patient were generated (table S1). CFS XMRV strains 1106 and 1178 each differed by 6 nt from the reference prostate cancer strain XMRV VP62 (EF185282), and with the exception of 1 nt, the variant nucleotides mapped to different locations within the XMRV genome, suggesting independent infections. In comparison, prostate cancer–derived XMRV strains VP35 and VP42 differed from VP62 by 13 and 10 nt, respectively. Thus, the complete XMRV genomes in these CFS patients

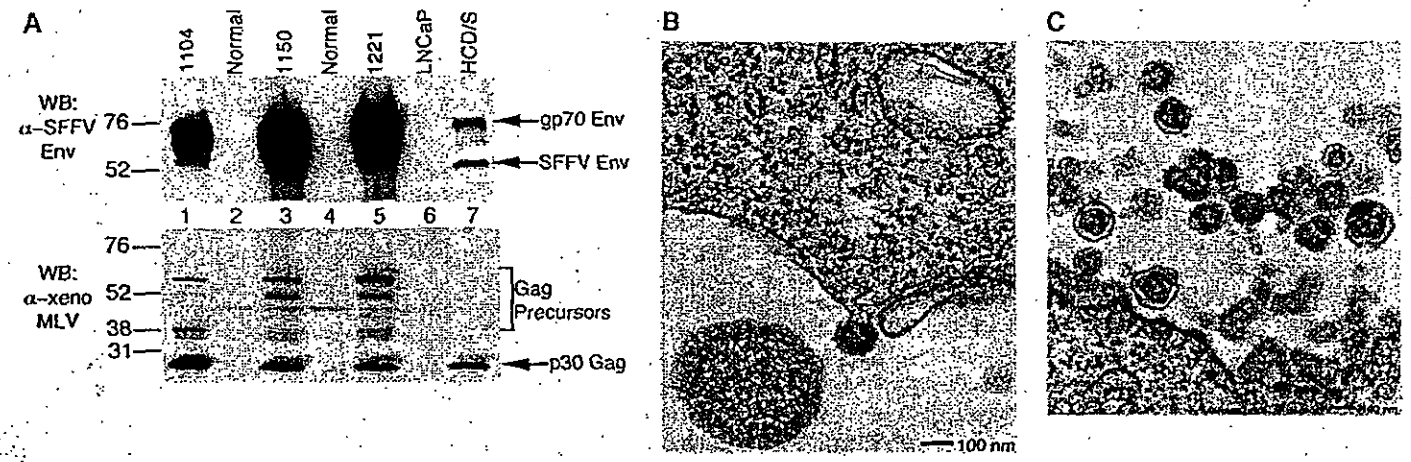

Fig. 3. Infectious XMRV in PBMCs from CFS patients. (**A**) Lysates of LNCaP cells cocultured with PBMCs from CFS patients (lanes 1, 3, and 5) or healthy donors (lanes 2 and 4) were analyzed by Western blots with rat mAb to SFFV Env (top panel) or goat antiserum to xenotropic MLV (bottom panel). Lane 6, uninfected LNCaP; lane 7, SFFV-infected HCD-57 cells. MW markers in kilodaltons are at left. (**B**) Transmission electron micrograph of a budding viral particle from LNCaP cells infected by incubation with an activated T cell culture from a CFS patient. (**C**) Transmission electron micrograph of virus particles released by infected LNCaP cells.

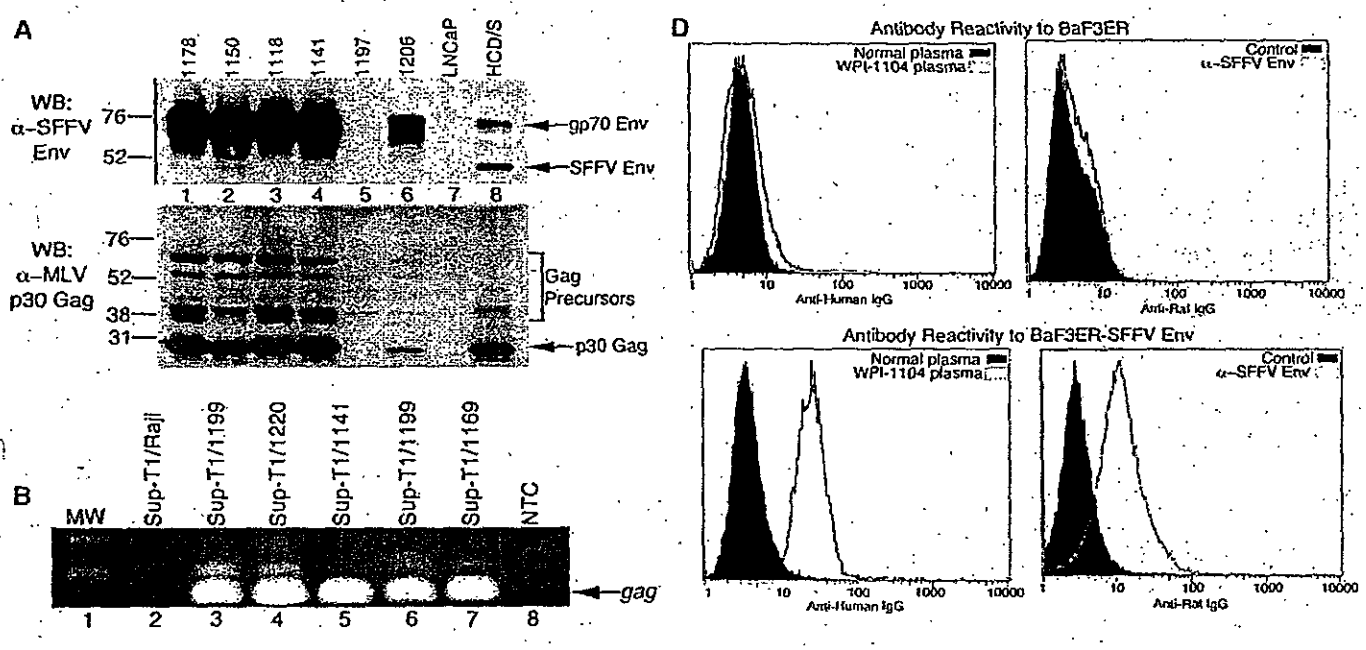

Fig. 4. Infectious XMRV and antibodies to XMRV in CFS patient plasma. (**A**) Plasma from CFS patients (lanes 1 to 6) were incubated with LNCaP cells and lysates were prepared after six passages. Viral protein expression was detected by Western blots with rat mAb to SFFV Env (top panel) or goat antiserum to MLV p30 Gag (bottom panel). Lane 7, uninfected LNCaP; lane 8, SFFV-infected HCD-57 cells. MW markers in kilodaltons are at left. (**B**) Cell-free transmission of XMRV to the SupT1 cell line was demonstrated using transwell coculture with patient PBMCs, followed by nested *gag* PCR. Lane 1, MW marker. Lane 2, SupT1 cocultured with Raji. Lanes 3 to 7, SupT1 cocultured with CFS patient PBMCs. Lane 8, no template control (NTC). (**C**) Normal T cells were exposed to cell-free supernatants obtained from T cells (lanes 1, 5, and 6) or B cells (lane 4) from CFS patients. Lanes 7 and 8 are secondary infections of normal activated T cells. Initially, uninfected primary T cells were exposed to supernatants from PBMCs of patients WPI-1220 (lane 7) and WPI-1221 (lane 8). Lanes 2 and 3, uninfected T cells; lane 9, SFFV-infected HCD-57 cells. Viral protein expression was detected by Western blot with a rat mAb to SFFV Env. MW markers in kilodaltons are at left. (**D**) Plasma samples from a CFS patient or from a healthy control as well as SFFV Env mAb or control were reacted with BaF3ER cells (top) or BaF3ER cells expressing recombinant SFFV Env (bottom) and analyzed by flow cytometry. IgG, immunoglobulin G.