The *MMWR* series of publications is published by the Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

Suggested Citation: Centers for Disease Control and Prevention. [Article title]. MMWR 2008;57:[inclusive page numbers].

A. phagocytophilum morulae in neutrophils. Retrospective review of an October 15 blood smear from the patient showed no evidence of intracellular morulae. Whole blood specimens from November 3–5 were positive for *A. phagocytophilum* DNA by PCR assays conducted at the Mayo Medical Laboratory, Minnesota Department of Health, and CDC. Serum from November 3–5 was tested at CDC and found to be weakly positive by indirect immunofluorescence assay (IFA) (titer 1:64) for immunoglobulin G (IgG) antibodies to *A. phagocytophilum*. Doxycycline treatment was begun on November 5. The patient's platelet count steadily improved and returned to a normal level of 163,000/mm^3 on November 10. Pretransfusion blood samples and serum from the patient's convalescence period were not available for further testing. The patient improved clinically and was transferred to a rehabilitation unit on November 13. After rehabilitation, the patient was discharged on December 3, 2007.

Epidemiologic and Laboratory Investigation

In early November, Memorial Blood Centers began an investigation to identify whether any of the 59 blood donors associated with the 34 RBC, 4 platelet, 14 FFP, and 7 cryoprecipitate units had evidence of *A. phagocytophilum* infection. Paired whole blood specimens from the original donations had been retained from all 34 RBC donors and eight of 14 FFP donors and were available for PCR testing. During November 2007–March 2008, Memorial Blood Centers also collected postdonation blood samples for serologic testing and information on recent illness history and potential tick exposure from 53 of the 59 donors. In addition, plasma components from two FFP donors and two cryoprecipitate donors who donated again during December 2007–January 2008 were retained for serologic testing. The whole blood specimens retained from initial donation were tested by PCR, followed by sequencing of the PCR amplicons at CDC. Serum and plasma specimens were tested by IFA for IgG antibodies to *A. phagocytophilum*.

PCR and IFA tests on samples from a female RBC donor aged 64 years were positive for *A. phagocytophilum* infection (Table). *A. phagocytophilum* DNA was found in an RBC product donated by this woman on September 28 and transfused to the patient on October 13. IgG IFA titers to *A. phagocytophilum* were 1:512 and 1:256, respectively, in subsequent sera collected November 17 and December 18. The donor did not recall being bitten by a tick, but had spent time in wooded areas of northeast Minnesota where anaplasmosis is endemic within the month before her donation. She reported no history of fever during the month before or after her donation. No other patients received blood components from her donation.

TABLE. Polymerase chain reaction (PCR) and immunofluorescence assay (IFA) results* for *Anaplasma phagocytophilum* testing of transfusion blood products from 59 donors — Minnesota, 2007

Blood product	PCR	IFA	No. of donors
Red blood cells (n = 34)	+	1:512†	1
	–	1:64	2
	–	<1:32	31
Apheresis platelets (n = 4)	NA§	<1:32	4
Fresh frozen plasma (n = 14)	–	<1:32	6
	–	NA	2
	NA	<1:32	6
Cryoprecipitate (n = 7)	NA	<1:32	7

* Results from PCR testing by CDC of 42 whole blood segments retained from the original donations and IFA testing of 57 serum or plasma specimens submitted after the original donation.
† IFA titers 1:64 and higher were considered positive.
§ Test results not available.

No whole blood samples from other tested donors were PCR positive for *A. phagocytophilum*. Sera from two RBC donors were weakly positive by IFA (titer 1:64), but their respective whole blood samples from the original transfused units were PCR negative. These two donors did not live on wooded property and reported they had no tick exposure or illness during the 2 months before donation. Available postdonation serum samples from other donors were negative for *A. phagocytophilum* by IFA (titer <1:32).

Reported by: *M Kemperman, MPH, D Neitzel, MS, Minnesota Dept of Health; K Jensen, J Gorlin, MD, E Perry, MD, Memorial Blood Centers, Saint Paul; T Myers, MD, T Miley, MD, Park Nicollet Methodist Hospital, Saint Louis Park, Minnesota. J McQuiston, DVM, ME Eremeeva, MD, PhD, ScD, W Nicholson, PhD, J Singleton, National Center for Zoonotic, Vector-Borne, and Enteric Diseases; J Adjemian, PhD, EIS Officer, CDC.*

Editorial Note: *A. phagocytophilum*, the causative agent of anaplasmosis, typically is transmitted to humans by infected *Ixodes* spp. ticks. In wooded areas of the United States, *A. phagocytophilum* is transmitted by the blacklegged tick (*Ixodes scapularis*) in the Northeast and upper Midwest and by the western blacklegged tick (*Ixodes pacificus*) on the West Coast. In infected persons who are symptomatic, illness onset occurs 5–21 days after a bite from an infected tick. Initial presentation typically includes sudden onset of fever, headache, malaise, and myalgia, often accompanied by thrombocytopenia, leukopenia, and elevated liver transaminases. Severe infections can include prolonged fever, shock, confusion, seizures, pneumonitis, renal failure, hemorrhages, opportunistic infections, and death (*1*). Anaplasmosis and other tickborne diseases, including human ehrlichiosis, Rocky Mountain spotted fever, and babesiosis, caused by *Ehrlichia chaffeensis* or *Ehrlichia ewingii*, *Rickettsia rickettsii*, and *Babesia* spp., respectively, represent a potential risk for transmission via blood transfusion in the United States (*2–6*).

The case described in this report provides strong presumptive evidence that *A. phagocytophilum* infection in this patient was acquired through blood transfusion. Pretransfusion blood samples and convalescent serum from the transfusion recipient were not available for PCR or serologic testing to demonstrate conclusively that the patient was free of *A. phagocytophilum* infection before his hospitalization on October 12. However, the patient reported limited outdoor exposure that might include potential tick contact during the 3 weeks before hospitalization, and a blood smear collected 3 days after hospital admission showed no evidence of intracellular morulae. The timing of events and the expected incubation period for anaplasmosis (5–21 days) suggest that the patient's exposure most likely occurred during hospitalization. *A. phagocytophilum* DNA was found in a retained sample from the implicated RBC product that was transfused to the recipient, providing strong evidence that this was the likely route of disease transmission to the blood transfusion recipient.

Some blood transfusion recipients (i.e., those who are immune compromised) likely are at increased risk for developing severe complications associated with tickborne diseases. Both *A. phagocytophilum* and *E. chaffeensis* can survive in refrigerated RBCs, and possible transfusion-transmission cases have been reported for anaplasmosis (Minnesota Department of Health, unpublished data, 1998) (*2,3,5,6*). However, because of the rarity of transfusion-associated cases, concerns regarding the specificity of available tests, (none of which are approved by the Food and Drug Administration), and the economic costs associated with implementation, the U.S. blood supply is not routinely screened for tickborne disease using laboratory methods (*7*).

As a method to reduce the risk for certain pathogens in blood products, blood banks often defer donations if the potential donor is ill at the time of donation. However, persons infected with tickborne disease might experience mild illness or have asymptomatic infection, as was the case with the implicated donor in this report (*1,3*). Screening donors for a recent history of tick bite is unlikely to identify high-risk donors, because this type of exposure frequently is not recalled by persons with anaplasmosis (*3*). In this case, the implicated donor did not recall a tick bite, although she did report contact with wooded habitat in an anaplasmosis-endemic area. Nearly 75% of the other blood donors in this investigation reported similar outdoor contact, making the screening of blood donors for tick-related exposures poorly predictive for possible infection. Because *Ehrlichia* and *Anaplasma* are associated with white blood cells, leukoreduction techniques would be expected to reduce the risk for *Ehrlichia* and *Anaplasma* transfusion-transmission through RBC components (*5,8*). In the absence of effective screening tools to identify donors or products infected with

the organisms, physicians should weigh the benefits of using leukoreduced blood components, to potentially reduce the risk for *Ehrlichia* and *Anaplasma* transmissions.

Although transfusion-associated transmission of *A. phagocytophilum* appears to be rare, reported incidences of anaplasmosis and other tickborne diseases are increasing in the United States (*1*). A record 322 cases of anaplasmosis were reported in Minnesota in 2007 (6.2 cases per 100,000 population) (*9*). As the incidence of tickborne diseases increases, physician vigilance for possible transmission of these agents via transfusions also should increase. In addition to other more common etiologies, physicians should suspect possible rickettsial infection if transfusion recipients develop acute thrombocytopenia posttransfusion, especially if accompanied by fever. Such signs should lead to rapid assessment for rickettsial agents and empiric treatment with doxycycline (*1*). Although insensitive, blood smear can provide timely support for a presumptive diagnosis of anaplasmosis, followed by IFA or PCR to confirm the diagnosis (*1*). Similarly, babesiosis should be suspected in patients who develop hemolytic anemia and fever posttransfusion (*3,4*).

Anaplasmosis and ehrliciosis are nationally notifiable diseases. Suspected cases of tickborne rickettsial diseases should be reported promptly to the state or local health department, and suspected transfusion-associated transmission should be reported to the supplying blood center and appropriate public health authorities.

Acknowledgments

The findings in this report are based, in part, on contributions by G Liu, PhD, and K Smith, DVM, PhD, Minnesota Dept of Health; M Kuehnert, MD, National Center for Preparedness, Detection, and Control of Infectious Diseases, and S Holzbauer, DVM, Coordinating Office for Terrorism Preparedness and Emergency Response, CDC.

References

1. CDC. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichiosis, and anaplasmosis—United States. MMWR 2006;55:(No.RR-4).
2. Eastlund T, Persing D, Mathiesen D, et al. Human granulocytic ehrlichiosis after red cell transfusion. Transfusion 1999;39:117S.
3. McQuiston JH, Childs JE, Chamberland ME, Tabor E. Transmission of tickborne agents of disease by blood transfusion: a review of known and potential risks in the United States. Transfusion 2000;40:274–84.
4. Herwaldt BL, Neitzel DF, Gorlin JB, et al. Transmission of *Babesia microti* in Minnesota through four blood donations from the same donor over a 6-month period. Transfusion 2002;42:1154–8.
5. McKechnie DB, Slater KS, Childs JE, Massung RF, Paddock CD. Survial of *Ehrlichia chaffeensis* in refrigerated, ADSOL-treated RBCs. Transfusion 2000;40:1041–7.
6. Kalantarpour F, Chowdhury I, Wormser GP, Aguero-Rosenfeld ME. Survival of the human granulocytic ehrlichiosis agent under refrigeration conditions. J Clin Microbiol 2000;38:2398–9.
7. AuBuchon JP. Meeting transfusion safety expectations. Ann Intern Med 2005;143:537–8.
8. Merrille FC, Salata KF, Belanger KJ, Casleton BG, Kelly DJ. Reducing the risk of transfusion-transmitted rickettsial disease by WBC filtration, using *Orientia tsutsugamushi* in a model system. Transfusion 2000;40:290–6.
9. CDC. Final 2007 reports of nationally notifiable infectious diseases. MMWR 2008;57:901, 903–13.

Progress in Introduction of Pneumococcal Conjugate Vaccine — Worldwide, 2000–2008

Pneumococcal disease is a leading cause of childhood morbidity and mortality globally, causing an estimated 0.7–1.0 million deaths annually among children aged <5 years (*1*). A pneumococcal conjugate vaccine (PCV) that includes seven pneumococcal serotypes (PCV7) first became available in 2000. Studies in the United States have demonstrated that introduction of universal vaccination with PCV7 resulted in a 77% decrease in invasive pneumococcal disease among children aged <5 years and a 39% decrease in hospital admissions for pneumonia among children aged <2 years (*2,3*). A similar vaccine with two additional serotypes was highly efficacious against pneumonia and invasive disease in clinical trials in Africa and, in one trial, reduced all-cause mortality among children by 16% (*4*). Low-income countries, which account for >97% of pneumonia cases in children aged <5 years (*5*), will benefit most from introduction of PCV. This report summarizes the progress made in introducing PCV7 worldwide. As of August 2008, 26 countries offered PCV7 to all children as part of national immunization programs or had PCV7 in widespread use (i.e., with estimated national coverage >50%); however, none of these countries is a low-income or lower-middle income country. The World Health Organization (WHO) and UNICEF have recognized the safety and effectiveness of PCVs and recommend that these vaccines for young children be included in national immunization programs (*1*). Overcoming the challenges to global introduction remains an urgent public health priority.

WHO recommends including PCV in national immunization programs (i.e., routine vaccination of all young children with PCV), particularly in countries where all-cause mortality among children aged <5 years is >50 per 1,000 live births or where >50,000 children die annually from any cause (*1*). In addition, because persons infected with human immunodeficiency virus (HIV) are up to 300 times more likely to have pneumococcal disease than those who are HIV negative (*6*), WHO recommends that countries with a high prevalence of HIV infection make the introduction of PCV a priority.

Only one PCV, the 7-valent formulation (PCV7), is currently licensed for use worldwide; new formulations of PCV (10-valent or 13-valent) are scheduled to become available

別紙様式第2-1

No. 30

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. 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		公表国
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)		ProMED 20080825.2648, 2008 Aug 25. 情報源:stuff.co.nz, New Zealand Press Association (NZPA) report, 2008 Aug 25.	WHO

研究報告の概要

○インフルエンザA型ウイルス(H1N1)、オセルタミビル耐性:南半球

タミフル(oseltamivir)耐性型の"通常の"季節性インフルエンザが急速に拡大しており、今年の冬(2008～2009)のインフルエンザ株の制御に当該薬剤が効果を示さない可能性がある。

H1N1株に感染した南アフリカ人患者107名全員がタミフルに耐性を示す変異株を保有していた。タミフルを服用していた患者は1名のみであった。

H1N1ウイルスの変異は、2007年の第4四半期～2008年3月31日に34カ国(主に北半球の国々)7528検体の検査では16%であったのに対し、2008年8月1日～20日の期間に、12カ国(主に南半球の国々)788検体の検査では、242名(31%)であった。

タミフル耐性型インフルエンザは、2007年1月に初めてノルウェーので蔓延がWHOに報告されて以来、ヨーロッパ、北米、南米、アフリカ、アジア、オーストラリアの40カ国で報告されている。

タミフル等の抗ウイルス製剤は、パンデミックが発現・蔓延後、ワクチンが開発されるまでの3ヶ月以上の期間、主要な治療手段であり、タミフルはWHOや世界各国の政府によって備蓄されている。

スウェーデンの研究者らは、ヒトで発症する別のウイルスと耐性型ウイルスが組み合わされた場合、タミフル耐性株に突然変異する可能性があると述べた。

使用上の注意記載状況・その他参考事項等

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

血液を介するウイルス、
細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
南アフリカをはじめとした南半球の各国において、タミフル(oseltamivir)耐性型の"通常の"季節性インフルエンザが急速に拡大しているとの報告である。	タミフル耐性インフルエンザウイルスが拡大しているという情報は、公衆衛生上及び血液事業への影響が大きく、厳重な注意が必要である。今後も引き続き情報の収集に努める。

(19)