EXHIBIT 47

The US Military Experience With Fresh Whole Blood During the Conflicts in Iraq and Afghanistan

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Abstract

Since its introduction in the early part of the last century, fresh whole blood (FWB) has been used by the US military as a battlefield expedient resuscitation method, even after the development of component therapy in the 1960s. In the recent conflicts in Iraq and Afghanistan, FWB was used once more, often collected in the setting of a walking blood bank (WBB). Considerable research and opinion from military circles has cited these experiences and sparked renewed interest in FWB as an effective resuscitation tool in the setting of trauma. Despite efforts by the US military to improve the effectiveness and safety of FWB through a series of widely published guidelines, transfusion transmitted infections (TTI) remain a vexing challenge. These experiences in Iraq and Afghanistan will help inform a larger discussion regarding the reintroduction of FWB in civilian trauma resuscitation.

Keywords

blood loss, coagulopathy, hemorrhage, noncardiac surgery, risk management

Introduction

According to the Armed Services Blood Program, in the recent military conflicts in Iraq and Afghanistan,* more than 28,000 wounded personnel were transfused nearly 300,000 blood products, over 9000 of which were whole blood units.[1] The purpose of this article is to explore the US military's policies and recent experience with whole blood transfusion during these conflicts. For the purposes of this article, whole blood is blood collected from a donor that is transfused without undergoing any fractionation; fresh whole blood (FWB) is whole blood that is less than 24 hours old and kept at room temperature[2,3]; and massive *transfusion* (MT) is transfusion the 10 or more units of blood to a single casualty within 24 hours.[4]

US Military's History With Whole Blood Transfusion

The first known human blood transfusion took place on June 15, 1667, when Dr Jean-Baptiste Denis (sometimes spelled "Denys") transfused several ounces of lamb's blood to a feverish young man who had been previously bled with leeches. The patient survived, but Denis's other transfusion experiments eventually led to a patient death. Denis was charged with murder but later exonerated when it was discovered that the patient may have been poisoned by his own wife. Nonetheless, the event led the French Parliament to ban all human blood transfusions, and similar actions followed throughout much of Europe.[5,6]

With these bans in place, little progress was made on human blood transfusion over the next few centuries. However, a series of events in the early part of the 20th century moved transfusion science forward significantly with the discovery of the 3 principal blood types by Dr Karl Lansteiner in 1901, the first blood transfusion using blood typing and cross-matching by Dr Reuben Ottenberg in 1907, and the development of long-term anticoagulants such as sodium citrate in 1914.[7]

The first military blood banking and transfusion occurred in 1917 during World War I by Lieutenant Oswald Robertson, a graduate student at the Rockefeller

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Foundation, recently commissioned in the US Medical Officer Reserve Corps. During the battle of Cambrai, Robertson stored 22 units of blood in a makeshift blood bank/ice chest crafted from 2 ammunition cans. Robertson used his device to successfully transfuse 20 severely wounded Canadian soldiers judged too deep in shock to risk surgery. Nine of his patients survived, and Robertson's transfusion methods became widespread among the British Expeditionary Force.[8]

Despite its popularity among British military surgeons, whole blood transfusion was not embraced in US military medical circles. At the start of World War II, US military medical authorities deemed whole blood transfusion too difficult and dangerous to perform in a combat theater, and "blood substitutes," such as plasma and later albumin, were used as the primary resuscitation fluid for hemorrhagic shock. In northern Africa, however, American physicians observed their British counterparts using whole blood to resuscitate badly wounded soldiers, and the practice began to take hold in US military circles.[9]

As the scale of US military involvement in the wars in Europe and the Pacific expanded, so too did its need for blood, exhausting donor supplies available in theater. Eventually, a plan was put in place to collect whole blood from Red Cross Donor Centers in the United States and airlift units to military hospitals in Europe and the Pacific. By the war's end, the Red Cross had provided more than 13 million pints of blood for use in the war effort as whole blood, as well as for the production of albumin and freeze-dried plasma.[10]

In the 5 intervening years between the end of World War II and the start of the Korean War, the military's blood program stagnated. As a consequence, the United States entered the Korean War without a formal blood program and did not ship any blood for the first 70 days of the conflict.[10] But during the 1960s, several important innovations moved transfusion science away from whole blood and closer to the component therapy (CT) used in today's modern operating room. In the early to mid-1960s, plasmapheresis was introduced as a method for collecting plasma for transfusion, and shortly thereafter packed red blood cells (pRBC) replaced whole blood as a primary means to supplement lost oxygen-carrying capacity. In 1969, S. Murphy and F. Gardner demonstrated the feasibility of storing platelets at room temperature, thus revolutionizing platelet transfusion therapy.[7] Blood storage methods were also further refined, in part to facilitate the safe shipment of blood products to US military hospitals in far-off Vietnam. Small amounts of whole blood were still collected in US military facilities in Vietnam to keep a ready supply of fresh platelets.[10]

In recent years, although generally replaced by component therapy, whole blood transfusion remained a "field expedient" resuscitation method for trauma in the US military. In the conflicts in Somalia[11] and Kosovo,[12] military physicians turned once more to FWB transfusion when CT was not readily available.

Whole Blood: The Ideal Resuscitation Fluid?

The move to CT in the setting of trauma, as outlined above, was not because CT was believed to be more efficacious than whole blood resuscitation. Rather, CT first took hold in elective surgeries on euvolemic patients, where it allowed for better storage and screening, and more judicious use of individual blood components. Once in place, whole blood simply became less and less available, leaving CT as the only option for trauma resuscitation. Thus, the transition to CT in the setting of hemorrhagic shock took place without any demonstration of its effectiveness as a resuscitation fluid over whole blood.[13]

Whole blood has great appeal in the setting of trauma, particularly in the setting of MT, as it "replaces what is bled." Indeed, if one were to administer blood components in ratios similar to whole blood (pRBC:FFP:PLT as 1:1:1; FFP stands for fresh frozen plasma and PLT stands for platelets), one is left with an anemic, cold, thrombocytopenic, diluted solution. Such a solution would be roughly 660 to 680 mL (roughly 280 mL of which is anticoagulants and additives), have a hematocrit of less than 30% with coagulation factors diluted to 60% of their usual concentration, and 80,000 platelets per microliter (only two thirds of which would be viable).[14] In contrast, a 500-mL unit of FWB has a hematocrit of roughly 33% to 43% with 86% activity of clotting factors, 130,000 to 350,000 platelets per microliter,[15] and contains only 60 to 70 mL of anticoagulants and additives.[16] Recent research indicates that while the pH and levels of 2,3-DPG (2,3-diphosphoglycerate) of whole blood diminish after 3 days at room temperature, plasma coagulation and PLT function are largely preserved.[17]

Another principal advantage of whole blood over CT is the avoidance of "storage lesion," or the degradation of stored blood with time, which is associated with a host of clinically significant adverse outcomes ranging from decreased red blood cell aggregation and 2,3-DPG activity, to an increased incidence of infection, multi-organ failure, and death.[17] Given the logistical challenges of far-off military campaigns, it is not surprising that storage lesion has been a vexing problem in Afghanistan and Iraq, where, early in the war, the average age of blood transfused at one combat support hospital was 33 days.[18]

Whole Blood Use in the Wars in Iraq and Afghanistan

In the earliest stages of the wars in Iraq and Afghanistan, surgical support for the troops engaged in combat was

highly mobile and flexible, much like the conflict itself. Transfusion requirements were met with blood products collected outside of theater and rapidly transported to US military medical facilities in the combat zone. As the conflict evolved, medical support and operating rooms became more stationary, and medical staff began to look internally to meet transfusion needs.

In the US military, care for the wounded is organized into 5 escalating levels, with level I care administered by the combat medic and at the austere "Battalion Aid Station," to level V care administered at large stateside military hospitals. Blood is first available in limited supply at level II, which is composed of Forward Surgical Teams (FSTs) and "Charlie Med" units, the latter of which may carry as much as 50 units of pRBCs.[19] Full transfusion capabilities of all blood components are available at level III care, or the Combat Support Hospitals (CSH). As these components run short, as is often the case with highly perishable platelets (5 days at room temperature),[20] these institutions sometimes turn to FWB.[15]

The third edition of *Emergency War Surgery*, a standard and revered text among military physicians, was published in the early stages of the wars in Iraq and Afghanistan. Within its highly readable and outlined text it describes the need for the "Walking Blood Bank" (WBB) contingency when blood and blood components are not readily available. A WBB uses FWB drawn from personnel (usually service members) in the vicinity for immediate transfusion. The chapter describes the steps involved in such a process and reminds the reader that "dog tags," on which is stamped a service member's blood type, are inaccurate 2% to 11% of the time and should only be used as a last resort. Several options for the conduct of a WBB are described depending on the austerity of the setting, from a CSH that has exhausted its supply of blood components, to medical personnel in very remote settings with limited medical supplies. In the latter setting, the manual describes the "white tile method" of cross-matching, using drops of blood from donor and recipient, waiting 4 minutes and examining the mixture with a hand lens to ensure there is no agglutinization.[2]

The whole blood transfusions that took place in Iraq and Afghanistan were not usually under such austere conditions, but were conducted at formal medical facilities and usually as a part of a larger resuscitation in which blood components, especially platelets, were in short supply. Massive transfusions are especially taxing on forward deployed military medical facilities with limited resources. The very busy CSH in Baghdad, Iraq (Ibn Sina) acquired the means to collect apharesis platelets (aPLTs) on-site in November of 2004.[21] Prior to this date, FWB remained an important source for platelets during massive transfusions.

The military's experience in the early years of the wars in Iraq and Afghanistan led to considerable research evaluating advantages and risks associated with FWB transfusion as well as high platelet/plasma to RBC ratio CT. Often retrospective, this research focused on casualties from the early to mid-portion of the conflicts (November 2003 to October 2007), often treated at the CSH in Baghdad (Ibn Sina). The conclusions drawn from these studies challenged conventional notions of trauma resuscitation, which had long called for crystalloid fluid and pRBCs upfront, and components such as plasma and platelets only when a set number of pRBCs had been transfused or when lab values demonstrated their need. The source of much of this research was the United States Army Institute of Surgical Research (USAISR) at Fort Sam Houston, Texas, an institution dedicated to providing requirements-driven combat casualty care medical solutions and products for injured soldiers, from self-aid through definitive care across the full spectrum of military operations.[22] At USAISR's disposal was the Joint Theater Trauma Registry (JTTR), an enormous and well-maintained repository of all Department of Defense trauma-related data.

One of the first of this series of studies was from Borgman et al[23] and looked at blood product ratios in 246 combat casualties who received massive transfusions at a CSH in Iraq. Borgman et al[23] demonstrated that a 1:1.4 ratio of plasma to RBCs was associated with improved overall mortality, as well as mortality from hemorrhage, when compared with casualties who receive plasma and RBCs in ratios of 1:2.5 and 1:8 (overall mortality rates were 65%, 34%, and 19%, respectively, $P < .001$; and hemorrhage mortality rates were 92.5%, 78%, and 37%, respectively, $P < .001$).

In a retrospective analysis of 708 combat casualties transfused at least one unit of blood product at a CSH in Iraq, Spinella et al[24] demonstrated that each transfused FFP unit was independently associated with increased survival (odds ratio = 1.17; 95% confidence interval = 1.06-1.29; $P < .002$); whereas each transfused pRBC unit was independently associated with decreased survival (odds ratio = 0.86; 95% confidence interval = 0.8-0.92; $P < .001$). In another retrospective analysis of 354 combat casualties who received either FWB, RBCs, plasma but not aPLTs versus casualties who received aPLTs, RBC, plasma but not FWB, Spinella et al[13] (a different research group than that referenced above) found improved 24-hour and 30-day survival with the FWB group (96% vs 88% $P = .018$; 95% vs 82%, $P = .002$). The authors posed several possible explanations for this benefit, to include the fact that FWB is more concentrated, and lacks both the anticoagulant additives and the storage lesions of reconstituted CT.

Perkins et al[25] undertook 2 retrospective analyses looking at the use of platelets in combat casualty resuscitations. The first study looked at the relationship between aPLT:RBC ratio and survival in 694 massive transfusions that included aPLT, but not FWB. At 24 hours, patients receiving a high ratio of aPLT:RBC (<1:8) had better

survival (95%) compared with patients receiving a medium ratio (1:16 to 1:8; survival = 87%) and patients receiving the lowest ratio of platelets (<1:16; survival = 64%; $P = .04$ and $P < .001$, respectively). The survival benefit for the high and medium ratio groups remained at 30 days as compared with those receiving the lowest ratio of platelets (75% and 60% vs 43%, $P < .001$ for both comparisons).[25]

In a separate study (with a slightly different research group), Perkins et al[21] looked at the source of platelets (aPLT vs FWB) in 369 massive transfusions of combat casualties. Unadjusted survival between the 2 groups was similar at 24 hours (84% vs 81%, respectively; $P = .52$) and at 30 days (60% vs 57%, respectively; $P = .72$). Multivariate regression failed to identify differences in survival between patients receiving PLT transfusions either as FWB or as aPLT at 24 hours or at 30 days. The authors, in addition to calling for prospective studies to evaluate the efficacy of FWB in civilian populations, concluded that FWB is a reasonable alternative to aPLTs in austere environments where standard component therapy is not available.[21]

In addition to these studies, several review articles and editorials published at about the same time cited the widespread and successful use of FWB in the conflicts in Iraq and Afghanistan. These articles cite the long history the US military has had using FWB in the setting of combat trauma, even after the development of component therapy. Underscoring the unique experience and limitations in resources of the military setting, these authors argue that, particularly in the setting of massive transfusion and resistant coagulopathy, FWB has been and should remain one of the tools available to clinicians treating combat casualties.[15,26,27]

The Safety of Whole Blood Transfusion

In the US military, the screening for transfusion transmitted infections (TTIs) of FWB has varied depending on the acuity of the situation in which it is used. In 1993, the 46th CSH performed 56 surgical procedures in 48 hours on the combat casualties of the Battle of the Black Sea in Mogadishu, Somalia. Eighty units of whole blood were transfused solely using dog tags to determine blood type, with no rapid screening tests for TTIs. Remarkably, this group reported no transfusion reactions, and, according to survivor screening once returning to the United States, no TTIs.[11] In *Emergency War Surgery*, third edition, the chapter on Shock and Resuscitation suggests that the safety of whole blood transfusion may be improved through planning, that is, developing a roster of donors prescreened for TTIs, with known blood and Rh types. In a mass casualty situation (when the number of casualties threaten to outstrip a medical facility's resources), the authors suggest reducing the confusion in the handling of blood by drawing only "O" type blood.[2]

As all US whole blood donors in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) were US Department of Defense (DoD) personnel, mandatory DoD vaccination and screening policies contributed considerably to the safety of FWB transfusion. All active duty US service members are screened for HIV every 2 years, and reserve component soldiers every 5 years.[28] Not long after the start of the OIF and OEF, USCENTCOM (US Central Command—the Unified Combatant Command over US Armed Forces in Central Asia, to include both OIF and OEF) mandated HIV rescreening of all deploying personnel 120 days prior to entering either theater of operation.[29] About the same time, the DoD mandated compulsory HBV immunization series for all new recruits into the armed forces.[30] Any service member with HIV, hepatitis C virus (HCV), hepatitis B virus (HBV), or human T-lymphotropic virus (HTLV) is barred from deployment.[29]

The safety of the FWB was further enhanced by a screening questionnaire. Since 1993, the Army used DD FORM 572 (version February 93) "BLOOD DONATION RECORD" as the screening tool for blood donors, which contained 32 questions addressing high-risk history and behavior. A modified version of this form (DD FORM 572 (WB)) was used for FWB donation, with 9 less questions (many of the nonapplicable questions, such as recent travel outside the United States, were removed) and extra wording at the bottom of the form reminding the donor that his or her donated blood would not be tested for viral disease prior to transfusion. Just prior to donation, donors were then tested for anemia using a copper sulfate test.[27]

Despite the final wording of DD FORM 572 (WB), efforts were in fact made during OIF and OEF to rapidly prescreen recently collected FWB for TTIs just prior to transfusion, although these efforts evolved over the course of the conflicts. Up until 2006, CSH laboratories had no standard TTI rapid screening test for FWB. Thus, in an effort to empirically improve the safety of FWB transfusion, from April to December 2004 the CSH in Baghdad used rapid immunochromatographic test kits purchased from Spain and shipped directly to the hospital. Because of limited availability of these kits, not all FWB could be screened.[18] Moreover, the sensitivity and specificity of the test kits, reported by the manufacturer to be between 98% and 99% for each test, was challenged by an independent analysis by O'Connell at the US Army Walter Reed Institute of Research.[15,31,32] The test kits have since been replaced with more reliable test kits.[3]

In addition to these immediate prescreening efforts samples were also collected from FWB donors and

transported back to the United States to undergo formal testing and tracking for HBV, HCV, rapid precipitation reaction (RPR), HTLV I/II, HIV by ELISA/Western blot, and nucleic acid testing for HIV and HCV.[27] All US recipients of FWB are required to undergo screening for TTIs initially and at 3, 6, and 12 months following transfusion.[11]

Repine et al[27] report that while the 31st CSH manned the hospital at Ibn Sina in Baghdad, Iraq, FWB collected in this manner could be delivered to the operating room within 1 hour of being requested. During periods when high numbers of casualties were anticipated, such as during the second battle of Fallujah (Operation Phantom Fury[33]) in November and December 2004, whole blood was collected in advance and stored at room temperature for up to 8 hours, after which most of it was in fact transfused. After 8 hours, the unused units were placed in cold storage (4°C) and marked as non-FWB, considered equivalent to one unit of pRBCs and one unit of FFP (no platelet activity).[27]

Several authors argue that although this method of collecting and transfusing whole blood does carry certain risks, it does in fact limit recipient exposure to donors. Mathematically, a recipient who is transfused a unit of PRBCs, a unit of FFP, and a unit of aPLTs has several fold greater donor exposure than does a recipient who receives a single unit of whole blood.[27]

In September 2007, an epidemiologic consultation team from the US Army Public Health Command conducted an investigation to determine the risk of TTIs among recipients of FWB and PLTs in OEF and OIF. Using stored pre- and posttransfusion sera, the consultation team tested for HCV, HIV, and HBV among some 470 US Service Members who received emergency transfusion products. Selected regions of viral genomes from epidemiologically linked infected recipients and their donors were sequenced and compared.

The team discovered a single case of transfusion transmitted HCV infection (incidence rate of 2.1/1000). Perhaps more alarming was the discovery of 4 cases of HCV and 2 cases of chronic HBV (no cases of HIV) among the pretransfusion sera of recipients. As these recipients were themselves members of the potential emergency donor population, this study seemed to better characterize the safety of FWB. Among the authors' conclusions was a call for rigorous application of existing in-theater countermeasures for screening emergency blood prior to transfusion, and, as an additional countermeasure, predeployment screening programs for HCV and HBV, like the ones already in place for HIV.[34]

Another risk associated with FWB transfusion is transfusion-associated microchimerism (TA-MC). Chimerism is the presence of more than one genetically distinct cell line in an organism that originated from one zygote, and microchimerism describes the phenomena when the allogenic cell population is small (<5%). TA-MC is chimerism when the new cell line originates from a blood donor in a blood recipient. Developments in polymerase chain reaction (PCR) techniques have contributed considerably to TA-MC studies and indicate that the phenomenon is more common in transfusion recipients who suffer severe traumatic injuries and massive hemorrhage, and receive relatively fresh blood products.[35] In a 2007 study undertaken by Utter et al,[36] TA-MC cell lines were found to persist in combat injured veterans from World War II and the Korean and Vietnam wars, in some cases 60 years after transfusion.[36]

In a study by Dunne et al,[37] prospective posttransfusion data were collected at >14 days on 26 severely injured combat casualties between December 2006 and March 2007. Among these patients, 4 were not transfused any blood products, and all 4 tested negative for microchimerism. However, TA-MC was present in 45% (10 of 22) patients who were transfused at least 1 unit of blood. The prevalence of TA-MC trended toward a higher risk among those who were transfused FWB or aPLTs: 50% (3 of 6) in FWB recipients, 50% (4 of 8) in recipients of platelets and only 38% (3 of 8) in those who only received pRBCs. However, the difference in the rate of TA-MC between the pRBC group and the FWB and aPLT groups did not reach clinical significance ($P = .60$ and $P = .38$, respectively). The authors advocate larger studies to tease out this trend, as well as to ascertain possible clinical consequences such as graft-versus-host disease or autoimmune disease syndromes, among patients with TA-MC.[37]

The Current State of Affairs: The Clinical Practice Guidelines

Among much of the valuable literature published by the USAISR are the "CENTCOM JTTS CPGs" (Central Command/Joint Theater Trauma System Clinical Practice Guidelines). These generally evidence-based guidelines represent the current thinking by the US military on a host of medical issues, to include the use of FWB. The CPG for FWB transfusion was first released in 2006 and has since undergone regular review, most recently in February 2011. The FWB CPG recommends reserving the use of FWB for casualties requiring massive transfusion, with clinically significant shock or coagulopathy (eg, bleeding with associated metabolic acidosis, thrombocytopenia or international normalized ratio >1.5), when optimal component therapy is unavailable or resuscitation with stored CT is not adequate (most likely at level I and II facilities), and there is an immediate threat of loss of life, limb, or eyesight. In facilities where full CT is available (eg, level III facilities), the CPG clearly states, given infectious concerns,

that "the risk:benefit ratio does not justify the routine use of FWB over banked blood products in non life-threatening severe trauma." However, when platelets and FFP inventories are depleted or exhausted, such as mass casualty situations, "the use of FWB remains an appropriate life-saving option."[3]

The FWB CPG describes the precautions involved in the use of FWB, much of which is achieved with the establishment of a prescreened pool of potential donors. Even with such a pool of donors in place, the CPG highly recommends the use of on-site rapid screening immunoassays for infectious disease (HIV, HBV, HCV) before FWB is transfused. In the appendix of this CPG, the precise steps of collecting FWB are described, to include performing "HIV, HCV, HBsAg, RPR, and as required, Malaria test, in accordance with the manufacturer's insert or standard operating procedure." In this same appendix, in the "Equipment and Materials" section for FWB collection and transfusion are listed the Oraquick ADVANCE Rapid HIV-1/2 Antibody Test, the Oraquick®HCV Rapid Antibody Test kit, and the OnSite HBsAg Rapid Test-Dip Strip (Serum/Plasma). The package insert for the OnSite HBsAg Rapid Test-Dip Strip lists a relative sensitivity of 96% and a relative specificity of 100%.[38] The literature contained in the OraQuick HCV Rapid Antibody Test and the Oraquick ADVANCE Rapid HIV-1/2 Antibody Test suggest sensitivities and sensitivities >96% in a high-risk population.[39,40]

Conclusion

Although the use of FWB waned with the advent of CT, it has remained a valuable tool in the repertory of battlefield physicians since its introduction in World War I. FWB was used once more by the US military in the austere operating rooms of Iraq and Afghanistan, where it again proved its effectiveness in resuscitation and correcting coagulopathy, particularly in the setting of massive transfusions. But like all instruments and strategies, FWB carries certain risks, such as the increased possibility of TTIs. These risks, however, must be considered in the context in which they were undertaken: the resource-limited massive resuscitation of a rapidly exsanguinating combat casualty. Those who have been party to such an effort can appreciate just how welcome FWB is, even with its risks, particularly when no other alternative is available.

Fortunately, the risk of TTI with FWB has been mitigated by a series of measures put in place by the US military, to include the rapid prescreening of freshly collected whole blood. Such improvements in safety may aid in the reintroduction of FWB in civilian trauma resuscitation, where resources may be less restricted, but where a product that offers all that FWB does would be no less welcome.

Author's Note

The US military conflict in Iraq began on March 20, 2003 and ended on December 18, 2011, and is referred to as both "Operation Iraqi Freedom" (OIF), and, since September 1, 2010, "Operation New Dawn" (OND). The US military conflict in Afghanistan began on October 7, 2001 and is referred to as "Operation Enduring Freedom" (OEF).

Declaration of Conflicting Interests

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EXHIBIT 48

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA

RICHARD ROE, *et al.*,

Plaintiffs,

v.

PATRICK M. SHANAHAN, *et al.*,

Defendants.

No. 1:18-cv-641-LMD-IDD

DECLARATION OF KEVIN CRON IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION

I, Kevin Cron, do hereby declare as follows:

1. I currently serve as the Preventive Medicine Officer and primary Waiver Action Officer for U.S. Central Command ("CENTCOM"), a theater-level Unified Combatant Command with responsibility for military operations across North Africa, Central Asia, and the Middle East, including Iraq and Afghanistan, within the Department of Defense ("DoD"). I have held this position since 2015. I act on behalf of the CENTCOM Surgeon to develop and interpret CENTCOM medical readiness standards and advise commanders and units on deployment issues, and have issued determinations for over 14,000 medical waiver applications, including applicants from all branches of the U.S. Armed Forces, as well as a variety of governmental, non-governmental, and contracting agencies. I am responsible for assessing wartime medical and environmental threats, integrating threat analyses into operational and strategic plans, and developing programs to minimize medically-related threats to USCENTCOM personnel, forces, and missions.

2. In the exercise of my duties, I have been made aware of this lawsuit by counsel from the DOD Office of the General Counsel.

3. I submit this declaration in support of the Defendant's Response to the Plaintiffs' January 11, 2018 Motion for a Preliminary Injunction. I base this declaration on my personal knowledge and on information made available to me in the performance of my duties. Unless specifically noted, the opinions in this declaration are my own and relate to my assigned duties within the CENTCOM Surgeon's office.

Purpose of this Declaration

4. This declaration is submitted in support of Defendant's Reply to Plaintiffs' Motion for a Preliminary Injunction. In their November January 11, 2019 Memorandum in Support of Plaintiff's Motion for a Preliminary Injunction, Plaintiffs state "'the military's restrictions on deployability are not rationally related to military effectiveness or readiness, because a person's physical capabilities are not generally affected by an HIV diagnosis."

Deployment Restrictions to the CENTCOM AOR

5. Deployment to the CENTCOM area of responsibility ("AOR") is governed by a variety of regulations, including Department of Defense Instruction ("DoDI") 6490.07 and Modification Thirteen to USCENTCOM Individual Protection and Individual-Unit Deployment Policy ("MOD 13").

6. DoDI 6490.07 (Deployment Limiting Medical Conditions for Service Members and DoD Civilian Employees) puts forth baseline guidance on medical deployability for the DoD. Enclosure 3 states, "In general, individuals with the conditions in paragraphs a. through h. of this enclosure, based upon a medical assessment as described in Enclosure 2 and Reference (l), shall not deploy unless a waiver is granted." Paragraph (e) (2) then states, "A diagnosis of human immunodeficiency (HIV) antibody positive with the presence of progressive clinical illness or immunological deficiency. The cognizant Combatant Command surgeon shall be

consulted in all instances of HIV seropositivity before medical clearance for deployment." Enclosure 4 additionally specifies Combatant Commanders shall "Serve as the final approval authority for exceptions to the medical standards (waivers) made pursuant to the procedures in this Instruction.", and serves as the basis for MOD 13.

8. MOD 13 is a CENTCOM policy, and provides guidance on medical readiness for deployment to the AOR. Paragraph 15.G.1 reiterates that, "the cognizant Combatant Command surgeon shall be directly consulted in all instances of HIV seropositivity before medical clearance for deployment." Tab A, Paragraph 7.C.2. clearly states that "Confirmed HIV infection is disqualifying for deployment". Paragraph 15.C of MOD 13 also notes that "Deployed health service support infrastructure is designed and prioritized to provide acute and emergency support to the expeditionary mission. All personnel (uniformed service members, government civilian employees, volunteers, DoD contractor employees) traveling to the CENTCOM AOR must be medically, dentally and psychologically fit." This is an important caveat that is considered in every waiver decision. MOD 13 also makes clear that "the final authority of who may deploy to the CENTCOM AOR rests with the CENTCOM Surgeon and/or the Service Component Surgeon's waiver authority, not the individual's medical evaluating entity or deploying platform."

9. The CENTCOM AOR presents many medical care challenges. The AOR covers 20 countries and covers more than 4 million square miles. Operations in the AOR are expeditionary in nature, and health service support plans are designed to meet the reasonably anticipated needs of a pre-screened warfighting population without complex medical needs. Conditions requiring highly specialized medical personnel, treatments, or medications cannot be reliably supported. Moreover, contingency deployments and deployment to austere conditions

may place Service members with mandatory medication or treatment regimens at risk because these regimens may be disrupted and may be difficult to replace in a timely manner. In the case of HIV treatment, such a disruption could result in the reactivation of the virus, with acquired resistance to the medication. This situation would place not only the individual Service member at risk, but also medical providers at all levels, including Host Nation and Coalition personnel, who may have to treat the Service member for battlefield injuries. The remaining force must also be considered, due to potential exposure to blood from treating, or being treated for, battlefield trauma, or for those individuals requiring battlefield blood transfusions.

10. In considering a medical waiver, I conduct an individual assessment of the risk each applicant poses to themselves, the deployed force, and, most importantly, the military mission in the CENTCOM AOR. The decision to grant a deployment waiver is a risk calculation that accounts for the applicant's condition, occupation, and time/location of deployment. We consider not only their current condition and stability, but also how they will be impacted by reasonably anticipated contingencies, such as loss, theft, or destruction of medication, how their condition will impact the evaluation of routine medical issues, what secondary effects their treatment may have, and how their condition will influence, and be influenced by, operational activities within active combat zones. It is a necessarily complex process. For a waiver to be granted, the needs of the Service to have the specific Service member or civilian in theater must be great enough to validate taking on this additional risk.

11. In my tenure as the wavier authority for CENTCOM, I have reviewed waiver requests from HIV-positive service members. I have not granted a deployment waiver for a HIV-positive Service member. After conducting a thorough risk assessment for each waiver request and consulting with the CENTCOM Surgeon and Component Surgeons, we determined

in each case that the risks of deploying a HIV-positive Service member were too great to justify waiver approval. It is highly unlikely that either Service member Roe or Voe would be granted a waiver to deploy to the CENTCOM AOR.

12. There are features of HIV which make it difficult to compare to other conditions. Treatment medications are highly specialized, and require constant, diligent compliance to be effective. A resurgent infection may go unnoticed, and must be considered as a possibility when other medical complaints arise. Currently, there is no cure for the disease. Medical conditions all have their own challenges, and must be considered in that context.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge and belief.

EXECUTED this 25th day of January 2019, Tampa, Florida.

LTC KEVIN CRON, MD, MPH
Preventive Medicine Officer
USCENTCOM/CCSG

EXHIBIT 49

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MMWR

Recommendations and Reports

August 1, 2008 / 57(RR06);1-19

Recommendations for Postexposure Interventions to Prevent Infection with Hepatitis B Virus, Hepatitis C Virus, or Human Immunodeficiency Virus, and Tetanus in Persons Wounded During Bombings and Other Mass-Casualty Events --- United States, 2008

Recommendations of the Centers for Disease Control and Prevention (CDC)

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The material in this report originated in the Coordinating Office for Terrorism Preparedness and Emergency Response, Rich Besser, MD, Director; the National Center for Immunizations and Respiratory Diseases, Anne Schuchat, MD, Director; the National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Kevin A. Fenton, MD, PhD, Director; the National Center for Preparedness, Detection, and Control of Infectious Diseases, Rima Khabbaz, MD, Director; the National Center for Injury Prevention and Control, Howard Frumkin, MD, Director, Division of Injury Response, Richard Hunt, MD, Director; and the National Institute for Occupational Safety and Health, John Howard, MD, Director.

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Summary

This report outlines recommendations for postexposure interventions to prevent infection with hepatitis B virus, hepatitis C virus, or human immunodeficiency virus, and tetanus in persons wounded during bombings or other events resulting in mass casualties. Persons wounded during such events or in conjunction with the resulting emergency response might be exposed to blood, body fluids, or tissue from other injured persons and thus be at risk for bloodborne infections. This report adapts existing general recommendations on the use of immunization and postexposure prophylaxis for tetanus and for occupational and nonoccupational exposures to bloodborne pathogens to the specific situation of a mass-casualty event. Decisions regarding the implementation of prophylaxis are complex, and drawing parallels from existing guidelines is difficult. For any prophylactic intervention to be implemented effectively, guidance must be simple, straightforward, and logistically undemanding. Critical review during development of this guidance was provided by representatives of the National Association of County and City Health Officials, the Council of State and Territorial Epidemiologists, and representatives of the acute injury care, trauma and emergency response medical communities participating in CDC's Terrorism Injuries: Information, Dissemination and Exchange (TIIDE) project. The recommendations contained in this report represent the consensus of U.S. federal public health officials and reflect the experience and input of public health officials at all levels of government and the acute injury response community.

Introduction

Public health authorities must consider how to provide care to injured persons in the event of acts such as bombings that result in mass casualties. During 1980--2005, of 318 acts of terrorism

investigated by the Federal Bureau of Investigation (FBI) in the United States or territories, 208 (65%) involved attempted bombings; of these 208 attempts, 183 (88%) succeeded. The majority of these acts were committed by domestic extremist groups that intentionally targeted property and did not cause deaths or injuries in persons; however, 19 bombings (10% of those that were successful) resulted in 181 deaths and 1,967 injured survivors. These figures do not include mass-casualty incidents that occurred outside the United States and its territories or those that occurred on U.S. soil that were classified as crimes, accidents, unintended negligence, or terrorist incidents other than bombings (e.g., the 2,972 persons killed as a result of the terrorist attacks of September 11, 2001). A total of 1,967 (91%) persons injured during terrorist bombings in the United States and approximately 12,000 (80%) persons injured during the terrorist attacks of September 11, 2001, survived (*1*).

Military health-care providers frequently must respond to mass-casualty events. During October 7, 2001--March 1, 2008, of 35,630 casualties incurred by U.S. Department of Defense forces involved in Operation Enduring Freedom (OEF) in Afghanistan and Operation Iraqi Freedom in Iraq (OIF), 27,441 (77%) resulted from mass-casualty events. Explosive devices accounted for 23,277 (65%) of these casualties. Of 27,441 persons wounded during OEF- and OIF-related mass-casualty events, 24,433 (89%) survived (U.S. Department of Defense, unpublished data, 2008).

In August 2001, the Israeli health ministry announced that tissue from two suicide bombers had tested positive for evidence of hepatitis B virus (HBV) (*2*). A 2002 case report from Israel described evidence of hepatitis B virus in a bone fragment that had traumatically implanted into a bombing survivor (*3*). Traumatically implanted bone fragments removed from five survivors of the 2005 London bombings were taken directly to forensic custody without testing for bloodborne pathogens (*4*) These observations support the potential for explosions to result in transmission of infections among persons injured during the event and indicate that emergency responders and health-care providers in the United States need uniform guidance on prophylactic interventions appropriate for persons injured in bombings and other events resulting in mass casualties. Wounds resulting from mass-casualty events require the same considerations for management as similar injuries resulting from trauma cases not involving mass casualties, including the risk for tetanus. In addition, exposure of wounds, abraded skin, or mucous membranes to blood, body fluids, or tissue from other injured persons (including suicide bombers and bombing casualties) might carry a risk for infection with a bloodborne virus. Injured survivors of mass-casualty events are at risk for infection with HBV, hepatitis C virus (HCV), or human immunodeficiency virus (HIV) and for tetanus.

Decisions regarding the administration of prophylaxis after a mass-casualty event are complex, and drawing direct parallels from existing guidelines regarding prophylaxis against bloodborne pathogens in occupational or nonoccupational settings is difficult. Assessment of risk factors commonly used to estimate the need for prophylactic intervention might not be possible in the setting of response to a mass-casualty event because responses to such events might overwhelm local emergency response facilities, and medical response staff will be focused primarily on rendering lifesaving trauma treatments. Because no uniform guidance existed for posstexposure interventions to prevent bloodborne infections and tetanus among U.S. civilians or military personnel wounded during mass-casualty event, CDC convened a Working Group comprising experts in injury response, immunizations, bloodborne infections, tetanus, and federal-, state-, and local-level public health response to develop such guidance.

The recommendations in this report pertain only to bombings and other mass-casualty events and are not meant to supplant existing recommendations for other settings. In a situation involving a substantial number of casualties, the ability to assess medical and vaccination histories or the risks

associated with the source of exposures might be limited, as might the supply of biologics. For this reason, in certain instances, the recommendations provided in this report differ from standard published recommendations for vaccination and prophylaxis in other settings. These recommendations are not meant to supplant existing recommendations for other settings and apply only to the specific situation of an event involving mass casualties. In addition, the recommendations provided in this report are limited to issues regarding initial postexposure management for bloodborne pathogens and tetanus prophylaxis. Other prophylactic measures that might be appropriate (e.g., use of antibiotics for the prevention of bacterial infection) are not discussed in this report.

Federal law requires the use of a Vaccine Information Statement (VIS) before the administration of vaccines against HBV or tetanus. VIS forms are available at http://www.cdc.gov/vaccines/pubs/vis/default.htm. Whenever feasible, a VIS form should be provided to patients or guardians before vaccination.

Individual states set forth their own legal requirements as to what constitutes the nature of informed consent that might be required before certain medical interventions. In general, these statutes also provide for exemptions in emergency circumstances. It is these state-specific laws that should guide response when informed consent would be applicable, but the circumstances of response to a mass-casualty event might preclude adherence to standard informed consent processes. Emergency responders and health-care providers should consult with their legal counsel for guidance regarding the relevant laws of their jurisdictions in advance of any mass-casualty event.

Methods

This report was developed through consultation among persons with expertise in immunization and other prophylactic interventions against bloodborne and other infections, physicians who specialize in acute injury-care medicine (trauma and emergency medicine), and local, state, and federal public health epidemiologists. Thus, the recommendations in this report represent the best consensus judgment of expert opinion.

This report adapts existing recommendations on the use of immunization and postexposure prophylaxis in response to occupational and nonoccupational exposures to bloodborne pathogens in the United States to the specific mass-casualty event setting while acknowledging the difficulty of drawing direct parallels. This adaptation also draws on guidance and practices developed previously and in use in the United Kingdom and Israel (*2,5--7*).

These recommendations were adopted through a process of expert consultation and consensus development. First, CDC drafted proposed preliminary recommendations on the basis of relevant existing U.S. guidance and practices of Israel and the United Kingdom (*2,5--7*). These proposed recommendations were discussed by representatives of the U.S. and international trauma response community at a May 2006 meeting in Atlanta, Georgia; following this discussion, the initial draft was revised. A working group then was convened comprising CDC staff members with expertise in injury response, tetanus, viral hepatitis, HIV infection, immunization and postexposure prophylaxis, and occupational safety and health, and representatives of the National Association of County and City Health Officials and the Council of State and Territorial Epidemiologists with experience in local and state level public health response. This group worked through the draft section by section to revise, update, and refine the recommendations; this revised document was shared again with representatives of the U.S. and international trauma response community for additional comment during a meeting in

Atlanta, Georgia, in August 2007. Because this guidance met the requirements established by the Office of Management and Budget (OMB) for a Highly Influential Scientific Assessment (HISA) (available at http://www.whitehouse.gov/omb/memoranda/fy2005/m05-03.html), the recommendations underwent a final process of external review in addition to undergoing internal CDC review for scientific content. As part of the OMB HISA peer review, the document was posted on CDC's website for public comment. An external expert panel subsequently reviewed and critiqued the document, the public comments, and CDC's response to those comments, and the document was revised a final time in response to the external review process.

Bloodborne Pathogens of Immediate Concern

Although transfusions and injuries from sharp objects (e.g., needlestick) have been associated with the transmission of multiple different pathogens (*8,9*), three bloodborne pathogens merit specific consideration in mass-casualty situations: HBV, HCV, and HIV. All three viruses are endemic at low levels in the United States and can be transmitted by exposure of infectious blood to an open wound or, more rarely, to skin abrasions or through exposure to intact mucous membranes. These viruses also can be transmitted by similar exposures to other body fluids or tissues from infected persons. Infection risks and options for postexposure prophylaxis vary, depending on the virus and the type of injury and exposure. Because hepatitis A virus (HAV) is transmitted via the fecal-oral route and is not considered a bloodborne pathogen (*10*), HAV prophylaxis is not recommended during a mass-casualty event.

The information typically used in occupational settings to guide prophylactic intervention decisions (including the circumstances of the injury, background prevalence of disease, or risk for infection of the source of exposure) might not be as clearly interpretable or as readily available in a mass-casualty setting. For example, both the extent of exposed disrupted skin and the volume of blood contributing to the exposure might greatly exceed that of usual occupational exposures. In addition, injured persons might be exposed to blood from multiple other persons or to biologic material from the body of a bomber or another injured person. The HBV, HCV, and HIV status of the source(s) usually will be unknown, and timely ascertainment might not be practical. If the circumstance in which each victim was injured can be characterized, this information can be used to assess the likelihood that an injured person was exposed to another person's blood. However, when such information is not readily available for persons injured during blast-related mass-casualty events, such blood exposure should be assumed.

Hepatitis B Virus

The prevalence of chronic HBV infection in the United States is approximately 0.4%. Prevalence varies by race, ethnicity, age group, geographic location, and individual history of risk behaviors (*11*).

Newly acquired HBV infection often is asymptomatic; only 30%--50% of children aged >5 years and adults have initial clinical signs or symptoms (*11*). The fatality rate among persons with reported cases of acute symptomatic hepatitis B is 0.5%--1.0% (*11*). No specific treatment exists for acute hepatitis B. Acute hepatitis B infection fails to resolve and instead progresses to chronic HBV infection in approximately 90% of those infected as infants, 30% of children infected at age <5 years, and <5% of persons infected at age ≥5 years (*11*). Overall, approximately 25% of persons who become chronically infected during childhood and 15% of those who become chronically infected after childhood die prematurely from cirrhosis or liver cancer (*11*). Therapeutic agents approved by

the U.S. Food and Drug Administration (FDA) for treating chronic hepatitis B can achieve sustained suppression of HBV replication and remission of liver disease for certain persons (*11*).

HBV is transmitted by percutaneous or mucosal exposure to infectious blood or body fluids. Although hepatitis B surface antigen (HBsAg) has been detected in multiple body fluids, only serum, semen, and saliva have been demonstrated to be infectious (*11*). Serum has the highest concentration of HBV, with lower concentrations in semen and saliva. HBV remains viable for 7 days or longer on environmental surfaces at room temperature (*11*). Among susceptible health-care personnel, the risk for HBV infection after a needlestick injury involving an HBV-positive source is 23%--62% (*12*). Prompt and appropriate postexposure prophylaxis (PEP) intervention reduces this risk. Many infections that occurred before widespread vaccination of health-care personnel probably resulted from unapparent exposures (e.g., inoculation into cutaneous scratches, lesions, or mucosal surfaces) (*12*).

Both passive-active PEP with hepatitis B immune globulin (HBIG) combined with hepatitis B vaccine and active PEP with hepatitis B vaccine alone have been demonstrated to be highly effective in preventing transmission after exposure to HBV (*12*). HBIG alone has been demonstrated to be effective in preventing HBV transmission. However, since hepatitis B vaccine became available, HBIG is used typically (and preferentially) as an adjunct to vaccination (*11*). The major determinant of effectiveness of PEP is early administration of the initial dose of vaccine (or HBIG). The effectiveness of PEP diminishes the longer after exposure it is initiated (*12*). Studies are limited on the maximum interval after exposure during which PEP is effective, but the interval is unlikely to exceed 7 days for perinatal and needlestick exposures (*12*). No data are available on the efficacy of HBsAg-containing combination vaccines when used to complete the vaccine series for PEP, but the efficacy of combination vaccines is expected to be similar to that of single-antigen vaccines because the HBsAg component induces a comparable antibody response (*12*). Antiviral PEP is not available for HBV.

A policy of liberal use of hepatitis B vaccine for PEP after bombings or in other mass-casualty situations is recommended because of the high concentration of HBV in blood of infected persons, the durability of HBV in the environment, and the efficacy and relative ease of administration of vaccine (*11*). Such use is consistent with existing recommendations for administering the hepatitis B vaccine series as PEP for persons (e.g., health-care personnel or sexual assault victims) exposed to a source with unknown HBV infection status (*11*,*12*). In general, PEP for HBV will be warranted for previously unvaccinated persons if wounds, nonintact skin, or intact mucous membranes might have been exposed to blood or body fluids from another person or persons. In a mass-casualty setting, failure to provide hepatitis B vaccination when needed could result in preventable illness, whereas unnecessary vaccination is unlikely to cause harm (*11*). Completion of primary vaccination at the time of discharge or during follow-up visits should be ensured for all persons who receive an initial hepatitis B vaccine dose as part of the acute response to a mass-casualty event.

If hepatitis B vaccine is in short supply, assessing how likely a person is to have been vaccinated previously might be necessary. In general, hepatitis B vaccination rates are highest among children aged <17 years (80%--90%) and health-care personnel (approximately 80%) (Table 1) (*13*--*15*) (see Pathogen-Specific Management Recommendations).

Hepatitis C Virus

The prevalence of chronic HCV infection in the United States is approximately 1.3% (*16*). Prevalence varies by race/ethnicity, age group, geographic location, and individual history of risk behaviors (*16,17*).

Persons with acute HCV infection typically either are asymptomatic or have a mild clinical illness. Antibody to HCV (anti-HCV) can be detected in 80% of patients within 15 weeks after exposure and in 97% of patients by 6 months after exposure. Chronic HCV infection develops in 75%--85% of infected persons. The majority remain asymptomatic until onset of cirrhosis or end-stage liver disease, which develops within 20--30 years in approximately 10%--20% of infected persons (*17*).

HCV is transmitted primarily through exposure to large amounts of blood or repeated direct percutaneous exposures to blood (i.e., transfusion or injection-drug use). HCV is not transmitted efficiently through occupational exposures to blood; the average incidence of anti-HCV seroconversion after accidental percutaneous exposure from an HCV-positive source is 1.8% (range: 0--7%), with one study indicating that transmission occurred only from hollow-bore needles (*17*). Transmission rarely occurs through mucous membrane exposures to blood, and in only one instance was transmission in a health-care provider attributed to exposure of nonintact skin to blood (*18*). The risk for transmission from exposure to fluids or tissues other than HCV-infected blood has not been quantified but is expected to be low. The exact duration of HCV viability in the environment is unknown but is at least 16--23 hours (*19,20*).

Immune globulin and antiviral agents are not recommended for PEP after exposure to HCV-positive blood. No vaccine against HCV exists. In the absence of PEP for HCV, recommendations for postexposure management are intended to achieve early identification of infection and, if present, referral for evaluation of treatment options. No guidelines exist for administration of therapy during the acute phase of HCV infection. However, limited data indicate that antiviral therapy might be beneficial when started early in the course of HCV infection. When HCV seroconversion is identified early, the person should be referred for medical management to a knowledgeable specialist (*12,17*).

Testing is not routinely recommended in the absence of a risk factor for infection or a known exposure to an HCV-positive source (*17*). However, current public health practice often does include advising testing for potential exposures to unknown sources (e.g., playground incidents involving needlestick or health-care exposures involving possible needle or syringe reuse or inadequately disinfected equipment). In the setting of a bombing or other mass-casualty event, both the extent of exposed disrupted skin and the volume of blood contributing to the exposure might greatly exceed that of usual occupational exposures. Thus, baseline and follow-up HCV testing should be considered for persons injured during bombings or other mass-casualty events whose penetrating injuries or nonintact skin are suspected to have come into contact with another person's blood or body fluids (see Pathogen-Specific Management Recommendations).

Human Immunodeficiency Virus

The overall prevalence of HIV infection in the United States was estimated to be 311.5 per 100,000 population (0.31%) in 2005, with wide geographic variability (range: 26.4 per 100,000 population [0.03%] [North Dakota]--2,060 per 100,000 population [2.06%] [Washington, DC]) (*21*). Prevalence might vary greatly among subpopulations within the same communities (e.g., residents of a nursing home compared with residents of transitional housing associated with a drug treatment program). The principal means of transmission in the United States is through sexual contact or through sharing of injection-drug use equipment with an infected person (*21*). Exposures also occur in occupational

settings (principally among health-care personnel) and infrequently can result in transmission. Guidelines for the use of antiretroviral PEP in both occupational and nonoccupational settings have been published previously (22--24), but these documents do not specifically address situations involving mass casualties.

Potentially infectious materials include blood and visibly bloody body fluids, semen, and vaginal secretions. Cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid also are considered infectious, but the transmission risk associated with them is less well defined. Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered infectious unless visibly bloody. Exposures that pose a risk for transmission include percutaneous injuries, contact of mucous membranes, or contact of nonintact skin with potentially infected fluids (22--24).

In studies of health-care personnel, the average risk for HIV transmission has been estimated to be approximately 0.3% (95% confidence interval [CI] = 0.2%--0.5%) after a percutaneous exposure to HIV-infected blood and approximately 0.09% (95% CI = 0.01%--0.5%) after a mucous membrane exposure. Transmission risk from nonintact skin exposure has not been quantified but is estimated to be less than that for mucous membrane exposure. Risk following percutaneous exposure is correlated positively with exposure to a larger quantity of blood, direct penetration of a vein or artery, a deep tissue injury, or exposure to blood from a source person with terminal illness (25), presumably related to high viral load.

Use of PEP with antiretroviral medications, initiated as soon as possible after exposure and continuing for 28 days, has been associated with a decreased risk for infection following percutaneous exposure in health-care settings (22). PEP also is recommended following nonoccupational sexual and injection-drug use--related exposures (24). Because of the potential toxicities of antiretroviral drugs, PEP is recommended unequivocally only for exposures to sources known to be HIV-infected. The decision to use PEP following unknown-source exposures is to be made on a case-by-case basis, considering the information available about the type of exposure, known risk characteristics of the source, and prevalence in the setting concerned.

In the majority of instances involving bombings or other mass-casualty events, the working group concluded that the risk for exposure to HIV-infected materials probably is low and that therefore PEP is not indicated. On this basis, PEP is not routinely recommended for treating persons injured in mass-casualty settings in the United Kingdom (7). For the same reason, HIV PEP should not be administered universally in mass-casualty settings in the United States unless recommended by the local public health authority. Such instances might occur for mass-casualty events in certain specific settings judged by public health authorities to be associated with higher risk for HIV exposure (e.g., a research facility that contained a large archive of HIV-infected blood specimens). In the rare situation in which PEP is recommended, it should be initiated as soon as possible after exposure, and specimens from the exposed person should be collected for baseline HIV testing. However, PEP should not be delayed for the results of testing. If PEP is used, certain other laboratory studies also are indicated. Consultation from health-care professionals knowledgeable about HIV infection is ideal, and is particularly important for pediatric patients and pregnant women. All persons for whom HIV PEP has been initiated should be referred to a clinician experienced in HIV care for follow up.

Tetanus

Clostridium tetani, the causative agent of tetanus, is ubiquitous in the environment and distributed worldwide. The organism is found in soil and in the intestines of animals and humans. When spores of *C. tetani* are introduced into the anaerobic or hypoaerobic conditions found in wounds or devitalized tissue, they germinate to vegetative bacilli that elaborate toxin and cause disease. This now infrequent but often fatal disease has been associated with injuries to otherwise healthy persons, particularly during military conflicts. During 1998--2000, the case-fatality ratio for reported tetanus in the United States was 18% (*26*). Although tetanus is not transmitted from person to person, contamination of wounds with debris might increase the risk for tetanus among persons injured in mass-casualty settings. Proper wound care and debridement play a critical role in tetanus prevention.

Serologic tests indicate that immunity to tetanus toxin is not acquired naturally. However, protection against tetanus is achievable almost universally by use of highly immunogenic and safe tetanus toxoid--containing vaccines. The disease now occurs almost exclusively among persons who were not vaccinated adequately or whose vaccination histories are unknown or uncertain (*27,28*). Universal primary vaccination, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, protects persons among all age groups.

The age distribution of recent cases and the results of serosurveys indicate that many U.S. adults are not protected against tetanus (*29*). The proportions of persons lacking protective levels of circulating antitoxins against tetanus increase with age; at least 40% of persons aged ≥60 years might lack protection. In the United States, tetanus is primarily a disease of older adults (*27,28*). Children are much more likely to have received age-appropriate vaccination; rates for receipt of 3 doses among children aged 19--35 months exceed 96% (*28*). During 1992--2000, only 15 cases of tetanus were reported in the United States among children aged <15 years. Parental philosophic or religious objection to vaccination accounted for the absence of immune protection for 12 (80%) affected children (*30*). Foreign-born immigrants, especially those from regions other than North America or Europe, also might be relatively undervaccinated (*29,31*).

Available evidence indicates that complete primary vaccination with tetanus toxoid provides long-lasting protection. After routine childhood tetanus vaccination, the Advisory Committee on Immunization Practices (ACIP) recommends routine booster vaccination with tetanus toxoid--containing vaccines every 10 years. For clean and minor wounds, a booster dose is recommended if the patient has not received a dose within 10 years. For all other wounds, a booster is appropriate if the patient has not received tetanus toxoid during the preceding 5 years.

In the setting of acute response to a mass-casualty event, failure to provide a tetanus vaccination when needed could result in preventable illness, whereas unnecessary vaccination is unlikely to cause harm (*26--29,32,33*). A substantial proportion of patients in this setting might be unable to provide a history of vaccination or history of contraindications to tetanus toxoid--containing vaccines, and the majority of wounds sustained will be considered tetanus-prone because they are likely to be exposed to dirt or feces. Thus, a wounded adult patient who cannot confirm receipt of a tetanus booster during the preceding 5 years should be vaccinated with tetanus and diphtheria toxoids vaccine (Td) or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap); adults aged ≥65 years should receive Td (*26*). Similarly, a child with an uncertain vaccination history should receive a tetanus booster as age-indicated by the standard childhood immunization table (pediatric diphtheria and tetanus toxoids and acellular pertussis vaccine [DTaP] if aged <7 years, Td if aged 7--10 years, and Tdap if aged ≥11 years) (*32,34*).

ACIP recommends that patients without a complete primary tetanus series who sustain a tetanus-prone wound routinely receive passive immunization with tetanus immune globulin (TIG) and

tetanus toxoid (*33*). In the setting of acute response to a mass-casualty event, many wounded patients probably will be unable to confirm previous vaccination histories, and thus TIG normally would be indicated. However, this might not be feasible in a mass-casualty setting if supplies of TIG are limited. All decisions to administer TIG depend on the number of casualties and the readily available supply of TIG. If the supply of TIG is adequate, consideration might be given to providing both tetanus toxoid and passive immunization with TIG at the time of management of tetanus-prone wounds. TIG is indicated if completion of a primary vaccination series is uncertain for an adult or if prior receipt of age-appropriate vaccinations is uncertain for a child. If TIG is in short supply, it should be reserved for patients least likely to have received adequate primary vaccination. In general, this group includes persons aged ≥60 years and immigrants from regions other than North America or Europe who might be less likely to have adequate antitetanus antibodies and who thus would derive the most benefit from TIG (*32*).

The TIG prophylactic dose that is recommended currently for wounds is 250 units administered intramuscularly (IM) for adult and pediatric patients. When tetanus toxoid and TIG are administered concurrently, separate syringes and separate sites should be used (*35*). In circumstances in which passive protection is clearly indicated but TIG is unavailable, intravenous immune globulin may be substituted for TIG. Postexposure chemoprophylaxis with antimicrobials against tetanus is not recommended.

ACIP recommends that adults and adolescents with a history of uncertain or incomplete primary vaccination complete a 3-dose primary series for tetanus, diphtheria, and pertussis (*26,30--34*). In the setting of acute response to a mass-casualty event, completion of the primary vaccination series of any vaccine provided initially during acute response during follow-up visits should be ensured at the time of discharge for inadequately vaccinated patients of all ages. Special precautions regarding management of pregnant women in the setting of emergency delivery have been identified (see Special Situations).

Recommendations

Risk Assessment

To determine appropriate actions in response to evaluation of casualties of bombings or other mass-casualty events, health-care providers should

- assess individual exposure risk by categorizing the patient into one of three exposure risk categories (Box 1) that are numbered sequentially from the highest (category 1) to the lowest (category 3) level of exposure risk and assign each person to the highest level risk category for which he/she qualifies,
- identify the appropriate risk category- and pathogen-specific management recommendation(s) (Box 1), and
- determine the appropriate action to take (see Pathogen-Specific Management Recommendations) in response to management recommendations.

When evaluating management choices for casualties of bombings or other mass-casualty events, health-care providers should assume that exposure to blood from other injured persons is likely unless available information on the circumstances of injury suggests otherwise. Blast injuries result occasionally in traumatic implantation of bone or other biologic material that is alien to the wounded person. Testing of such matter is not recommended as a useful adjunct for clinical management of

wounded persons. Public health authorities can provide assistance in assessing exposure risk for affected groups of injured persons. Tetanus risk is not dependent upon blood exposure.

Pathogen-Specific Management Recommendations

Hepatitis B Virus

Unless an injured person who is unable to communicate an accurate medical history or for whom medical records are not readily available is accompanied by a person able to function as a health-care proxy, responders should assume the absence of a reliable hepatitis B vaccination history and no contraindication to vaccination with hepatitis B vaccine (see Contraindications and Precautions). If administration of hepatitis B vaccine to a large number of persons after a mass-casualty event is anticipated to result in shortages of hepatitis B vaccine products, or if such shortages already exist, assistance with vaccine supply is available (see Vaccine Supply).

Recommendation: Intervene:

- Persons for whom neither a reliable history of completed vaccination against HBV nor a known contraindication to vaccination against HBV exist should receive the first dose of the HBV vaccine series as soon as possible (preferably within 24 hours) and not later than 7 days after the event.
- Persons who receive or are identified as candidates for a dose of hepatitis B vaccine while undergoing evaluation or treatment in immediate response to a mass-casualty event should be discharged with referrals for follow-up and written information on predischarge treatment to facilitate the ability of primary health-care providers to evaluate and, if appropriate, initiate or complete age-appropriate vaccinations or vaccination series (Appendix 1).

Recommendation: No action:

- No action is necessary to prevent HBV infection.

Hepatitis C Virus

Recommendation: Consider testing:

- Testing should be considered when an HCV-infected source is known or thought to be likely on the basis of the setting in which the injury occurred or exposure to blood or biologic material from a bomber or multiple other injured persons is suspected.
- Public health authorities can provide assistance in assessing exposures and therefore treatment for affected groups of injured persons. A decision to perform testing of specific persons might be made on the basis of the judgment of the treating physician and the preferences of the individual patient; testing during a follow-up referral might be a more feasible logistical option in the setting of response to a mass-casualty event.

If a decision is made to perform testing:

- baseline testing for anti-HCV and alanine aminotransferase (ALT) should be performed within 7--14 days of the exposure;
- follow-up testing for anti-HCV and ALT should be performed 4--6 months after exposure to assess seroconversion, preferably arranged as part of discharge planning;

- HCV RNA testing should be performed at 4--6 weeks if an earlier diagnosis of HCV infection is desired; and
- positive anti-HCV with low signal-to-cutoff value should be confirmed using a more specific supplemental assay before communicating the results to the patient; and
- persons who are tested or are identified as a candidate for testing regarding exposure to HCV while undergoing evaluation or treatment in immediate response to a mass-casualty event should be discharged with a referral for follow-up and written information on pre-discharge treatment (Appendix 1).

Recommendation: Generally no action:

- Exposure of mucous membranes to blood from a source with unknown HCV status generally poses a minor risk for infection and does not require further action.
- However, in settings in which exposure to an HCV-infected source is known or thought to be highly likely, testing for early identification of HCV infection following mucous membrane exposure may be considered. The decision to perform testing should be made on the basis of the judgment of the treating physician and the preference of the individual patient.

Recommendation: No action

- No action is necessary to prevent HCV infection.

Human Immunodeficiency Virus

Recommendation: Generally no action:

- In general, HIV PEP is not warranted. HIV PEP might be considered only in settings in which exposure to an HIV-infected source is known or thought to be highly likely (e.g., a blast injury incident that occurred in a research facility that contained a large archive of HIV infected blood specimens).
- HIV PEP should not be administered universally in response to mass-casualty events unless recommended by the local public health authority.
- In the rare event that HIV PEP is considered, it should be initiated as soon as possible after exposure. The patient should be counseled about the availability of PEP and informed of the potential benefits and risks and the need for prompt initiation to maximize potential effectiveness. If PEP is thought to be indicated on the basis of exposure risk, administration should not be delayed for HIV test results. Specific guidance on how to administer HIV PEP in unusual circumstances when it is warranted is available (see Special Situations).
- Persons who receive or are identified as candidates for HIV PEP while undergoing evaluation or treatment in immediate response to a mass-casualty event should be discharged with referrals for urgent follow-up. Written information on predischarge treatment should be provided to facilitate a primary health-care provider's ability to evaluate and, if appropriate, complete age-appropriate vaccinations or vaccination series (Appendix 1).
- In all health-care settings, opt-out screening for HIV (performing HIV screening after notifying the patient that the test will be performed, with assent inferred unless the patient declines or defers testing) is recommended for all patients aged 13--64 years. In the setting of response to a mass-casualty event, testing during a follow-up referral might be a more feasible logistic option unless a decision to administer PEP has been made (*35*).

Recommendation: No action:

- No action is necessary to prevent HIV infection.

Tetanus

All persons who sustain tetanus-prone injuries in mass-casualty settings should be evaluated for the need for tetanus prophylaxis. Tetanus-prone injuries include but are not limited to puncture and other penetrating wounds with the potential to result in an anaerobic environment (wounds resulting from projectiles or by crushing) and wounds, avulsions, burns, or other nonintact skin that might be contaminated with feces, soil or saliva.

All persons who are not accompanied by either medical records or a health-care proxy and whose ability to communicate an accurate medical history is uncertain for any reason should be deemed to lack a reliable tetanus toxoid vaccination history and to have no contraindication to vaccination with tetanus toxoid (see Contraindications and Precautions). If compliance with recommendations is anticipated to result in a shortage of tetanus toxoid products or TIG, assistance with product supplies is available (see Vaccine Supply).

Recommendation: Intervene:

- Appropriate wound care and debridement are critical to tetanus prevention.
- Age-appropriate vaccines should be used if possible. However, in a mass-casualty setting, this might not be possible, and any tetanus vaccine formulation might be used, because the tetanus toxoid content is adequate for tetanus prophylaxis in any age group. In this setting, the benefit of supplying tetanus prophylaxis outweighs the potential for adverse reactions from formulations from a different age indication.
- Adult patients who cannot readily confirm receipt of a tetanus booster during the preceding 5 years and who do not have known contraindication to tetanus vaccination should be vaccinated with Tdap (or with Td if Tdap is unavailable) or with Td if aged ≥65 years.
- Pediatric patients with uncertain vaccination history and with no known contraindication to tetanus vaccination should receive a tetanus booster according to the following schedule:
  --- DTaP if aged <7 years
  --- Td if aged 7--10 years
  --- Tdap (or Td if Tdap is unavailable) if aged ≥11 years.
- In a mass-casualty situation, unusually high demand might result in shortages of age-specific vaccine formulations, and logistic considerations might make differentiating patients by age category prohibitive. If supplies of DTaP are inadequate, heath-care providers might consider substituting Tdap or Td for DTaP because the amount of tetanus toxoid in all formulations is adequate to induce an immune response in a child. Similarly, if supplies of Td are inadequate, health-care providers might consider substituting Tdap for Td for persons aged ≥65 years. Pediatric DTaP generally is not indicated in persons aged ≥7 years; the increased diphtheria toxoid content is associated with higher rates of local adverse reactions in older persons (*26*,*32*). However, in a mass-casualty setting, other options might not exist.
- TIG might be indicated if completion of a primary vaccination series is uncertain for an adult, or prior receipt of age-appropriate vaccinations is uncertain for a child.
  --- If TIG is in short supply, use of TIG should be reserved first for persons aged ≥60 years and for immigrants from regions other than North America or Europe. All decisions to administer TIG depend on the number of casualties and the readily available supply of TIG.
  --- The recommended prophylactic dose of TIG is 250 units IM for adult and pediatric patients. When tetanus toxoid and TIG are administered concurrently, separate syringes and separate sites should be used (*34*).

- Persons who receive or are identified as candidates for tetanus toxoid--containing products or TIG while undergoing evaluation or treatment in immediate response to a mass-casualty event should be discharged with referrals for follow-up if possible. Written information on predischarge treatment should be provided to facilitate the ability of primary health-care providers to evaluate and, if appropriate, complete age-appropriate vaccinations or vaccination series (Appendix 1).

Recommendation: No action:

- No action is necessary to prevent tetanus. Exposure to blood or other bodily fluids generally is not considered a risk factor for tetanus.
- However, responders or persons engaged in debris clean up and construction are candidates for prophylaxis even if they do not sustain any wounds. When feasible, as a routine public health measure, tetanus toxoid vaccination with Tdap or Td should be offered to all persons whose last tetanus toxoid--containing vaccine was received ≥10 years previously and who either are responders or are engaged in either debris clean-up or construction and who thus might be expected to encounter further risk for exposure (*36--39*).

Vaccine and Antitoxin Supply

Adherence to these recommendations might increase the acute demand for tetanus toxoid--containing vaccine, TIG, and hepatitis B vaccine beyond the available local supply. In that event, local authorities might have to rely on local and state health departments, mutual aid agreements, or commercial vendors to supplement the supply of needed biologic or pharmaceutical products. If a local authority's capacity to respond to an emergency is exceeded and other local or regional resources are inadequate, local and state public health jurisdictions can, through their established communication channels for health emergencies, work with CDC and others as appropriate to assist with product shortages.

CDC's Strategic National Stockpile (SNS) maintains bulk quantities of pharmaceutical and nonpharmaceutical medical supplies for use in a national emergency. Tetanus toxoid, tetanus immune globulin, and hepatitis B vaccine are not included in the stockpile formulary. However, SNS has purchasing agreements for acquiring medical materials in large quantities, subject to commercial availability. CDC maintains stockpiles of pediatric vaccine products purchased by the Vaccines for Children Program that might be used to assist state, territorial, and tribal health departments in meeting emergent local demands for vaccines. CDC also can work with manufacturers and with state and local health authorities to assist with supply of vaccines that are not available in either the SNS or other CDC vaccine stockpiles.

Counseling

Hepatitis B and C Viruses

Persons undergoing postexposure management for possible exposure to HBV- or HCV-infected blood do not need to take any special precautions to prevent secondary transmission during the follow-up period (*12*,*17*). The exposed person does not need to modify sexual practices or refrain from becoming pregnant. An exposed nursing mother might continue to breastfeed. However, exposed persons should refrain from donating blood, plasma, organs, tissue, or semen until follow-up testing by the health-care provider has excluded seroconversion (*12*,*17*).

Human Immunodeficiency Virus

Persons known to be exposed to HIV should refrain from blood, plasma, organ, tissue, or semen donation until follow-up testing by the health-care provider has excluded seroconversion. In addition, measures to prevent sexual transmission (e.g., abstinence or use of condoms) should be taken, and breastfeeding should be avoided until HIV infection has been ruled out (*22*).

Special Situations

When HIV PEP is Initiated

HIV PEP should be considered only under exceptional circumstances. In the rare event that HIV PEP is considered, it should be initiated as soon as possible after exposure. The patient should be counseled about the availability of PEP and informed about the potential benefits and risks and the need for prompt initiation to maximize potential effectiveness. If PEP is thought to be indicated on the basis of exposure risk, administration should not be delayed for HIV test results.

In the rare event that HIV PEP is administered, specimens should be collected for baseline HIV testing on all patients provided with PEP using a blood or oral fluid rapid test if available; otherwise, conventional testing should be used. Testing should be discussed with the patient if the patient's medical condition permits. Procedures for testing should be in accordance with applicable state and local laws. PEP can be initiated and test results reviewed at follow-up. If the HIV test result is positive, PEP can be discontinued and the patient referred to a clinician experienced with HIV care for treatment.

If PEP is administered, the health-care provider also should obtain baseline complete blood count, renal function, hepatic function tests, and, in women, a pregnancy test. Because efavireniz might be teratogenic, it should not be administered until pregnancy test results are available (*12*,*22*). Otherwise, test results need not be available before PEP initiation but should be reviewed in follow-up.

Selection of antiretroviral regimens should aim for simplicity and tolerability. Because of the complexity of selection of HIV PEP regimens, consultation with persons having expertise in antiretroviral therapy and HIV transmission is strongly recommended. Resources for consultation are available from the following sources:

- local infectious diseases, hospital epidemiology, or occupational health consultants;
- local, state, or federal public health authorities;
- PEPline at http://www.nccc.ucsf.edu/Hotlines/PEPline.html, telephone 888-448-4911;
- HIV/AIDS Treatment Information Service at http://aidsinfo.nih.gov; and
- previously published guidance (see Information Sources).

Nevirapine should not be included in HIV PEP regimens because of potential severe hepatic and cutaneous toxicity. Efavirenz should not be used if pregnancy is known or suspected because of potential teratogenicity (*12*,*22*).

PEP should be started as soon after exposure as possible and continue for 4 weeks. For ambulatory patients, a starter pack of 5--7 days of medication should be provided, if possible. Alternatively, for

hospitalized patients, the first dose should be taken in the emergency department, and follow-up orders should be written for completion of the course in the hospital.

Patients on PEP should be reassessed for adherence, toxicity, and for follow-up of HIV testing (if rapid testing was not available at baseline) within 72 hours by an infectious disease consultant. Patients continuing on PEP should have follow-up laboratory evaluation as recommended previously (*22*--*24*), including a complete blood count and renal and hepatic function tests at baseline and at 2 weeks postexposure, and HIV testing at baseline, 6 weeks, 3 months, and 6 months postexposure.

Persons begun on HIV PEP should be discharged with written instructions and a referral to ensure follow-up care with a clinician experienced with HIV care and information on the age-appropriate dose and schedule (Appendix 1).

Simultaneous Administration

When tetanus toxoid and TIG are administered concurrently, separate syringes and separate anatomic sites should be used (*40*). Hepatitis B vaccine and tetanus toxoid--containing vaccines might be administered at the same time using separate syringes and separate sites (*36*).

Treatment with an antimicrobial agent generally is not a contraindication to vaccination (*40*). Antimicrobial agents have no effect on the responses to vaccines against tetanus or hepatitis B.

Administration of Blood Products

The administration of hepatitis B vaccine or tetanus toxoid--containing products does not need to be deferred in persons who have received a blood transfusion or other blood products.

Pregnancy

Pregnancy is not a contraindication to vaccination against hepatitis B. Limited data suggest that a developing fetus is not at risk for adverse events when hepatitis B vaccine is administered to a pregnant woman. Available vaccines contain noninfectious HBsAg and should cause no risk for infection to the fetus (*11*).

Pregnancy is not a contraindication for HIV PEP. However, use of efavirenz should be avoided when pregnancy is known or suspected (*11*,*22*).

Pregnant adolescents and adults who received the most recent tetanus toxoid--containing vaccine ≥5 years previously generally should receive Td in preference to Tdap when possible (*41*).

Responders and Other Personnel

Responders and persons engaged in debris removal or construction often are at risk for incurring wounds throughout the duration of response and clean up work. As a routine public health measure, health-care providers should offer tetanus toxoid vaccination to all response workers who do not have a reliable history of receipt of a tetanus toxoid--containing vaccine during the preceding 10 years, regardless of whether the health-care visit was for a wound (*38*,*39*). Such persons might encounter potential exposure situations throughout the duration of their work in response to a mass-casualty situation.

Health-care personnel, emergency response, public safety and other workers (e.g., construction workers and equipment operators) who are injured and exposed to blood while providing assistance after a mass-casualty event should be managed according to existing guidelines and standards for the management of occupational exposures (*10,22,42*). Health-care personnel and first responders whose activities involve contact with blood or other body fluids should have been previously vaccinated against HBV and tetanus (*12,22*).

Contraindications and Precautions

Hepatitis B Vaccine

Hepatitis B vaccination is contraindicated for persons with a history of anaphylactic allergy to yeast or any vaccine component (*11*). On the basis of CDC's Vaccine Study Datalink data, the estimated incidence of anaphylaxis among children and adolescents who received hepatitis B vaccine is 1 case per 1.1 million vaccine doses distributed (95% CI = 0.1--3.9) (*11*). Persons with a history of serious adverse events (e.g., anaphylaxis) after receipt of hepatitis B vaccine should not receive additional doses. Vaccination is not contraindicated in persons with a history of multiple sclerosis, Guillain-Barré syndrome, autoimmune disease (e.g., systemic lupus erythematosis or rheumatoid arthritis), or other chronic diseases (*11*).

Antiretroviral Therapy

Nevirapine should not be included in HIV PEP regimens because of potential severe hepatic and cutaneous toxicity. Efavirenz should not be used if pregnancy is known or suspected because of potential teratogenicity (*12,22*).

Preparations Containing Tetanus Toxoid

The only contraindication to preparations containing tetanus toxoid (TT, Td, or Tdap) is a history of a neurologic or severe allergic reaction following a previous dose. Local side effects alone do not preclude continued use (*26,30,31*). If a person has a wound that is neither clean nor minor and for which tetanus prophylaxis is indicated, but also a contraindication to receipt of tetanus toxoid--containing preparations, only passive immunization using human TIG should be administered.

Reporting Adverse Events

Vaccine Adverse Events Reporting System

Any clinically significant adverse events that occur after administration of any vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS) even if causal relation to vaccination is uncertain. The National Childhood Vaccine Injury Act requires health-care providers to report to VAERS any event listed by the vaccine manufacturers as a contraindication to subsequent doses of the vaccine or any event listed in the Reportable Events Table (available at http://vaers.hhs.gov/reportable.htm) that occurs within the specified period after vaccination. VAERS reporting forms and information can be requested 24 hours a day at telephone 800-822-7967 or by accessing VAERS at http://vaers.hhs.gov. Web-based reporting also is available, and providers are

encouraged to report adverse events electronically at http://secure.vaers.org/VaersDataEntryintro.htm.

Reporting Adverse Events Associated With Antiretroviral Drugs and TIG

Unusual or severe toxicities believed to be associated with use of antiretroviral agents or TIG should be reported to FDA's MEDWATCH program (http://www.fda.gov/medwatch) at MedWatch, HF-2, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; telephone 800-332-1088.

National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (NVICP) was established by the National Childhood Vaccine Injury Act and became operational on October 1, 1988. Intended as an alternative to civil litigation under the traditional tort system (in that negligence need not be proven), NVICP is a no-fault system in which persons thought to have suffered an injury or death as a result of administration of a covered vaccine may seek compensation. Claims may be filed on behalf of infants, children and adolescents, or by adults receiving VICP-covered vaccines. Other legal requirements (e.g., the statute of limitations for filing an injury or death claim) must be satisfied to pursue compensation. Claims arising from covered vaccines must be adjudicated through the program before civil litigation can be pursued. The program relies on a Reportable Events Table listing the vaccines covered by the program and the injuries, disabilities, illnesses, and conditions (including death) for which compensation might be awarded. Additional information about NVICP is available at http://www.hrsa.gov/vaccinecompensation or from the National Vaccine Injury Compensation Program, Health Resources and Services Administration, Parklawn Building, Room 11C-26, 5600 Fishers Lane, Rockville, MD 20857; telephone 800-338-2382.

Information Sources

Recommendations for immediate prophylactic interventions have been summarized (Table 2). Recommendations for issues that might arise in association with immediate prophylactic intervention also have been summarized (Table 3).

In addition to the guidance provided in these recommendations, information on specific vaccines or other prophylactic interventions also is available (Box 2). ACIP recommendations regarding vaccine use are published by *MMWR*. Electronic subscriptions are available free of charge at http://www.cdc.gov/subscribe.html. Printed subscriptions are available at Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402-9235, telephone 202-512-1800.

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Table 1

TABLE 1. Estimated percentage of persons vaccinated against hepatitis B virus infection, by age group and selected characteristics — United States, 2001–2006

Group	No. doses	% vaccinated	(95% CI*)	Source
Infants aged 19–35 mos	3	93.4	(92.8–94)	National Immunization Survey, 2001–2006†
Adolescents aged 13–17 yrs	3	81.3	(79.4–83.1)	National Immunization Survey, 2001–2006§
Adults aged 18–49 yrs	≥1	34.6	(33.5–35.6)	National Health Interview Survey, 2004¶
Health-care personnel	≥1	80.5	(77.3–83.4)	
Police/firefighters	≥1	63.3	(56.6–70.1)	
Adults at high risk**	≥1	45.4	(41.7–49.2)	

* Confidence interval.
† CDC. National, state, and local area vaccination coverage among children aged 19–35 months—United States, 2006. MMWR 2007;56;880–5.
§ CDC. National vaccination coverage among adolescents aged 13–17 years—United States, 2006. MMWR 2007;56;885–8.
¶ CDC. Hepatitis B vaccination among adults—United States, 2004. MMWR 2006;55:509–11.
** Includes persons who reported having a sexually transmitted disease other than human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome during the previous 5 years, persons who consider themselves at high risk for HIV infection, and persons who reported any one of the following risk factors: hemophilia with receipt of clotting factor concentrates, men who have sex with men, injection-drug use, trading sex for money or drugs, testing positive for HIV, or having sex with someone with any of these risk factors.

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Box 1

BOX 1. Recommended postexposure management by risk category and specific pathogen

Risk category	HBV*	HCV†	HIV§	Tetanus
Category 1. Penetrating injuries or nonintact skin exposures¶	Intervene	Consider testing	Generally no action	Intervene
Category 2. Mucous membrane exposures**	Intervene	Generally no action	Generally no action	No action
Category 3. Superficial exposure of intact skin††	No action	No action	No action	No action

* Hepatitis B virus.
† Hepatitis C virus.
§ Human immunodeficiency virus.
¶ Penetration of skin by a sharp object that was in contact with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue) before penetration. Nonintact skin exposure is defined as contact of nonintact skin with any of these potentially infectious tissues or fluids.
** Contact of mucous membranes (i.e., eyes, nose, mouth, or inner surfaces of the gut or genital areas) with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue).
†† Superficial exposure of intact skin (but not of mucous membranes) with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue).

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Table 2

TABLE 2. Summary of recommendations for immediate prophylactic intervention

Type of injury or blood exposure	HBV*	HCV†	HIV§	Tetanus
Category 1. Penetrating injury/nonintact skin¶	For persons for whom no reliable history of hepatitis B vaccination exists and for whom no contraindication to vaccine is known, initiate hepatitis B vaccine series, preferably within 24 hours and not later than 7 days.	No prophylaxis recommended. Consider testing (immediately or during a follow-up referral) if exposure is to a known or likely HCV-infected source or multiple sources. If testing is performed, obtain baseline (within 7-14 days) and follow-up (4–6 months) anti-HCV and ALT.	Generally, no PEP** is warranted; consider only if exposure is to a known or highly likely HIV-infected source.	Clean and debride wound as appropriate. Give age-appropriate tetanus toxoid vaccine if date of receipt of last dose is unknown and no known history of vaccine contraindication exists. May consider administering TIG (in addition to tetanus toxoid) if no reliable history of tetanus primary series exists (always use separate syringes and separate administration sites). If TIG is in short supply, persons aged ≥60 yrs and immigrants from regions other than Europe or North America are most likely to derive benefit.
Category 2. Mucous membranes††	For persons for whom no reliable history of hepatitis B vaccination exists and for whom no contraindication to vaccine is known, initiate hepatitis B vaccine series, preferably within 24 hours and not later than 7 days.	Generally no action. Testing for early identification of HCV infection following mucous membrane exposure should be considered only in settings in which exposure to an HCV-infected source is known or thought to be highly likely.	Generally, no PEP** is warranted. Consider only if exposure is to a known or highly likely HIV-infected source.	No action
Category 3. Superficial exposure of intact skin††	No action	No action	No action	No action

* Hepatitis B vaccine.
† Hepatitis C vaccine.
§ Human immunodeficiency virus.
¶ Penetration of skin by a sharp object that was in contact with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue) before penetration. Nonintact skin exposure is defined as contact of nonintact skin with any of these potentially infectious tissues or fluids
** Postexposure prophylaxis. HIV PEP rarely is indicated. If PEP is indicated, the following procedures should be undertaken: 1) PEP should be started as soon as possible after exposure, without waiting for HIV test results; 2) PEP should be continued for 4 weeks; 3) Specimens should be collected for baseline testing, including HIV, complete blood count, liver function, creatinine, and pregnancy tests; 4) testing should be conducted in accordance with applicable state and local laws; 5) expert consultation should be obtained; sources of expert consultation include local persons with infectious diseases, hospital epidemiology, or occupational health expertise; local, stage, or federal public health authorities; PEPline (available 24 hours/day via telephone 1-888-448-4911 [preferred] or online at http://www.ncoc.ucsf.edu/Hotlines/PEPline.html; or the HIV/AIDS Rx information service at http://aidsinfo.nih.gov; 6) PEP should be continued for 4 weeks; 7) the patient should be discharged with written information, a 5–7 day supply of medication, and a follow-up appointment; and, 8) an HIV specialist should reassess the patient's condition within 72 hours.
†† Contact of mucous membranes (i.e., eyes, nose, mouth, or inner surfaces of the gut or genital areas) with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue).
†† Superficial exposure of intact skin (but not of mucous membranes) with blood, tissue, or other potential infectious body fluid (i.e., semen, vaginal fluid, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid or any other visibly bloody body fluid or tissue).

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Box 2

BOX 2. Online information sources

Vaccines

Advisory Committee on Immunization Practices (ACIP) recommendations, available at http://www.cdc.gov/vaccines/pubs/ACIP-list.htm.

CDC vaccines and immunization website, available at http://www.cdc.gov/vaccines.

American Academy of Pediatrics (AAP) Red Book, available at http://aapredbook.aappublications.org.

Downloadable Vaccine Information Statements, available at http://www.cdc.gov/vaccines/pubs/vis/default.htm.

Childhood, adolescent and adult immunization tables

Harmonized childhood, adolescent and adult immunization tables, available at http://www.cdc.gov/vaccines/recs/schedules/default.htm.

Postexposure prophylaxis (PEP) against HIV

CDC. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States. MMWR 2005;54(No. RR-2). Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm.

CDC. Updated U.S. Public Health Service guidelines for management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR 2001;50 (No. RR-11). Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm.

CDC. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis. MMWR 2005;54(No. RR-9). Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.htm.

CDC. Notice to readers: updated information regarding antiretroviral agents used as HIV postexposure prophylaxis for occupational HIV exposures. MMWR 2007;56:1291–2. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5649a4.htm.

PEPline, available 24-hours/day at telephone 888-448-4911 (preferred) or at http://www.ucsf.edu/hivcntr/Hotlines/PEPline.html.

HIV/AIDS Treatment Information Service, available at http://aidsinfo.nih.gov.

Postexposure Prophylaxis (PEP) Against HBV and HCV in Occupational Settings

CDC. Updated U.S. Public Health Service guide-

lines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR 2001;50(No. RR-11). Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm.

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Table 3

TABLE 3. Summary of recommendations for issues in special situations potentially associated with immediate prophylactic intervention

Issue/Situation	HBV*	HCV†	HIV§	Tetanus
Vaccine supply shortage	Local public health departments, mutual aid agreements, or commercial vendors should be relied on.If local capacity is exceeded, local public health authorities should work through established communication channels with CDC and others.	NA¶	NA	Age-appropriate vaccines are preferred. If age-appropriate vaccine supply is expended, any tetanus vaccine formulation may be used, as the tetanus toxoid content is adequate for tetanus prophylaxis in any age group. In this setting, the benefit of supplying tetanus prophylaxis outweighs the potential for adverse reactions from formulations from a different age indication. Local public health departments, mutual aid agreements, or commercial vendors should be relied on. If local capacity is exceeded, local public health authorities should work through established communication channels with CDC and others.
Counseling	Exposed persons should refrain from donating blood, plasma, organs, tissue, or semen.	Exposed persons should refrain from donating blood, plasma, organs, tissue, or semen.	Exposed persons should refrain from donating blood, plasma, organs, tissue, or semen. In addition, persons known to be exposed to HIV should avoid breastfeeding and organ/tissue donation and take precautions to avoid sexual transmission until HIV infection has been ruled out.	NA
HIV PEP** is initiated	NA	NA	HIV PEP rarely is indicated. If it is, recommended procedures should be followed.††	

* Hepatitis B vaccine.
† Hepatitis C vaccine.
§ Human immunodeficiency virus.
¶ Not applicable.
** Postexposure prophylaxis.
†† If PEP is indicated, the following procedures should be undertaken: 1) PEP should be started as soon as possible after exposure, without waiting for HIV test results; 2) PEP should be continued for 4 weeks; 3) specimens should be collected for baseline testing, including HIV, complete blood count, liver function, creatinine, and pregnancy tests; 4) testing should be conducted in accordance with applicable state and local laws; 5) expert consultation should be obtained; sources of expert consultation include local persons with infectious diseases, hospital epidemiology, or occupational health expertise; local, stage, or federal public health authorities; PEPline (available 24 hours/day at telephone 1-888-448-4911 [preferred] or at http://www.ncoc.ucsf.edu/Hotlines/PEPline.html; or the HIV/AIDS Rx information service, available at http://aidsinfo.nih.gov; 6) PEP should be continued for 4 weeks; 7) the patient should be discharged with written information, a 5–7 day supply of medication, and a follow-up appointment; and 8) an HIV specialist should reassess the patient's condition within 72 hours.

TABLE 3. (*Continued*) Summary of recommendations for issues in special situations potentially associated with immediate prophylactic intervention

Issue/Situation	HBV	HCV	HIV	Tetanus
Simultaneous administration	HBV vaccine and tetanus toxoid can be administered concurrently; use separate syringes and anatomic sites.	NA	NA	Separate syringes and anatomic sites should be used for concurrent administration of TIG§§ and tetanus toxoid.
Administration of blood products	Receipt of blood products does not require deferral of vaccination.	NA	NA	Receipt of blood products does not require deferral of vaccination.
Pregnancy	Pregnancy is not a contraindication to HBV vaccination.	NA	Pregnancy is not a contraindication to HIV PEP. Efavirenz should be avoided if pregnancy is suspected.	Td is preferred to Tdap for pregnant adolescents and adults who received their most recent tetanus toxoid product >5 yrs previously.
Responders and other personnel	Workers should be managed according to existing guidelines for management of occupational exposures.	Workers should be managed according to existing guidelines for management of occupational exposures.	Workers should be managed according to existing guidelines for management of occupational exposures.	Tetanus toxoid vaccination should be offered proactively if no reliable history exists of a booster within the past 10 years; unwounded workers remain at risk for wounds throughout response.
Contraindications and precautions	Vaccine is contraindicated if history of anaphylactic allergy to yeast or to any vaccine component or of serious adverse event after prior receipt of HBV vaccine.	NA	Nevirapine should not be used for HIV PEP because of liver toxicity. Efavirenz should not be used if pregnancy is known or suspected. Persons with HIV PEP expertise should be consulted if possible.	Contraindicated if history of neurologic or severe allergic reaction to a previous dose. If wound is at risk and vaccine is contraindicated, TIG should be used.
Reporting adverse events	Vaccine Adverse Events Reporting System (VAERS), telephone, 1-800-822-7967 or http://vaers.hhs.gov.	NA	MEDWATCH http://www.fda.gov/medwatch or telephone 1-800-332-1089.	VAERS, telephone 1-800-822-7967 or http://vaers.hhs.gov. MEDWATCH http://www.fda.gov/medwatch or telephone 1-800-332-1088.
National Vaccine Injury Compensation Program	Health Resources and Services Administration (HRSA), telephone 1-800-338-2382 or http://www.hrsa.gov/vaccinecompensation.	NA	NA	Health Resources and Services Administration (HRSA), telephone 1-800-338-2382 or http://www.hrsa.gov/vaccinecompensation.

§§ Tetanus immune globulin.

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EXHIBIT 50

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

NICHOLAS HARRISON, ET AL.,

Plaintiffs,

vs. Case No. 1:18-CV-00641-LMB-IDD

PATRICK SHANAHAN, IN HIS OFFICIAL CAPACITY AS ACTING SECRETARY OF DEFENSE, ET AL.,

Defendants.

Washington, D.C.
Wednesday, February 13, 2019

Deposition of:

LT. COL PAUL TUMMINELLO

called for oral examination by counsel for Plaintiffs, pursuant to notice, at the office of Winston & Strawn, 1700 K Street, N.W., Washington, D.C., before KAREN LYNN JORGENSON, RPR, of Capital Reporting Company, beginning at 9:02 a.m., when were present on behalf of the respective parties:

CONTENT

TUMMINELLO DEPOSITION EXHIBITS

(Exhibits attached to transcript.)

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* * * * *

A And I'll do the same.
Q And we'll both try.
A Yes.
Q So what is -- what are the risks to HIV-positive service members incident to military service?
MS. BERMAN: I'm going to object again to scope. He's here to testify about waivers and exception to policy.
But you can answer to the extent you can answer that question.
THE WITNESS: There's -- there's a lot of risks involved with any disease state that a person has. So with HIV, there's always risk of infecting someone else. And there's inherent risks with anybody that has any kind of disease that can compromise their ability to perform their tasks.
Because when you go down -- when you're deployed -- and all soldiers need to be deployable -- so if you're deployed, there -- there is higher risks to the individual

if they have any disease state in which could worsen if they're not given the care and given the appropriate monitoring, whatever that may be, depending on what their disease state is, and how far along it is, and how often you have to monitor it.

And along with that, there's logistic issues that are related to getting their medications that are needed for -- any -- whatever chronic illness or injury that a person may have. All those things go into decision-making.

BY MR. SCHOETTES:

Q And, in addition, can you tell me what the concerns are with respect to the safety of the blood supply?

MS. BERMAN: Same objection.

THE WITNESS: Well, a soldier that has a chronic bloodborne pathogen is not able to give blood. So depending on -- the way the Army deploys certain -- in certain scenarios and austere environments, they rely on the blood supply that's on foot, which is another -- another

soldier. So, obviously, that would be one of the people that can't give blood. So they -- would you want to have that person deployed with you if they can't do what part of every soldier in that outfit is -- or unit is -- is obliged to do? So I guess that would be one of the -- the issues that would be -- would be considered.

BY MR. SCHOETTES:

Q And are there other conditions -- I think you referred to more generally a chronic bloodborne --

A Pathogen.

Q -- pathogen that would prevent a person from giving blood?

A Hepatitis C.

Q I was just asking if there are other situations --

A Yes.

Q -- where a person would not be able to give blood?

A Yes.

Q And do people -- are people allowed to

benefit analysis. If we have more than enough soldiers doing a certain, specific job, and then we have some more that want to come in and they don't meet exactly the standard, then they -- there is no -- we don't have to give them a waiver. There's no -- it's not something that you have to do as a service.

So if you do that risk analysis of an HIV individual, they're a high risk. So as such, they are not allowed to come in newly accessed into the service because of that risk. Because they are -- because it -- we know -- we wouldn't bring them in as a regular solider. They would be brought in to fall into a whole program that developed only for soldiers that were already in the service. We're not -- there's no need to grow that program. Every program that you have in the military costs money. So you run out of money to take care of those soldiers that you already have, i.e., the HIV patients that we then can't -- we can't care for them, so we're now going to change our policy.

Q And you just referred to access into the military, but it is true that you also cannot get a waiver to access and commission as an officer if you are not already in the military; isn't that correct?

A Same standard.

Q The -- so I understand there's not a right to obtain a waiver, but the waiver you've just described about the eye surgery is based on an individualized assessment of that person's medical condition, correct?

A I -- I guess, yes. Yes.

Q But for people living with HIV, it is a blanket decision or policy that they cannot obtain a medical waiver to access; is that correct?

A I believe it's regulation, right. Yes.

Q So, yes?

A Yes.

Q And it doesn't really matter if they have a progressive clinical illness or immunological deficiency, they are still not going to be able to get a waiver to access?

A Correct.

Q You're speaking or answering on behalf of the Army National Guard. Do you know if the Army has the authority to waive HIV for accession?

MS. BERMAN: Objection. Outside the scope.

THE WITNESS: That probably -- I suspect it's DoD level. I don't work for the Army.

BY MR. SCHOETTES:

Q Okay. Can you go back to Exhibit 4, which is AR40-501, and look to Page 2 under Paragraph 1-6H?

(Thereupon, the court reporter clarified.)

THE WITNESS: Hotel.

BY MR. SCHOETTES:

Q H, as in hotel.

And H says, "Waivers for enlistment" -- I'm sorry, "Waivers for initial enlistment or appointment, including entrance and retention in officer procurement programs, will not be granted if the applicant does not meet the

transmission for any viral illness is your eyes transmit things the easiest because there's just no barrier. So when some -- if someone were to suffer a catastrophic injury like that, that's one of the concerns for those kinds of things.

Q Do you have -- do you know what kind of exposure there needs to be quantitatively through the eyes to HIV in order for transmission to occur?

A I don't.

Q Do you know if this opinion from Colonel Morgan regarding transmissibility through combat situations takes into account the effects of successful treatment on the risk of transmission?

MS. BERMAN: Objection. Calls for speculation.

THE WITNESS: Yeah. I would be speculating.

BY MR. SCHOETTES:

Q He then goes on to say, "The medications required to control the primary condition do not

allow individuals to be stationed overseas where these medications cannot be guaranteed."

Can you tell me what the basis for that statement is?

A So I think we discussed earlier about deploying personnel and getting them medications. So there's common illnesses, and there's uncommon illnesses, and there's -- all medication has to be maintained under a certain temperature and things like that. So temperature variants can have an effect on medication.

If you get into a position in -- especially battlefield and austere environments, you never know when someone -- when the soldiers will be cut off or not be able to get supplies for long periods of time. And the supply chain is not such that it's going to happen overnight. We don't -- there's no FedEx or anything out there. So you just can't -- the mail may come and get to you two months after it was sent. It depends on the ships and things like that that are coming in.

All those things are made in the

decision -- I think we talked earlier about COMPOs and where we deploy folks and how long -- you know, whether that extra screen, if you will, so it's -- so suffice it to say, logistics is the problem.

Q Does the military provide other medications that service members take on a daily basis?

A They -- they do. Not -- so what happens is a soldier takes a certain amount of medications with them when they deploy, and common medications, will be -- they may be get resupplied. However, the soldiers that are deployed and taking medications, those soldiers are only allowed to deploy if them not taking their medications will not adversely affect them in any way for a -- up to a year.

Q And that's the -- that's the demarcation point, is if they can go without medication for a year without any detrimental effects?

A I -- I don't have that -- no. That is not the demarcation point. I'm not sure what the

you -- you know, if you have the same answer, it's the same answer.

But what is the likelihood that Sergeant Harrison would deploy to a combat zone as a member of the D.C. National Guard JAG corps?

MS. BERMAN: Same objections.

THE WITNESS: And it's the same answer. We're all subject to deployment.

BY MR. SCHOETTES:

Q What is the likelihood that Sergeant Harrison would see any combat in any deployment as a member of D.C. National Guard JAG corps?

MS. BERMAN: Same objections.

THE WITNESS: And how many folks have died -- I'm not going to say that.

So we no longer have battlefield rules where there's a frontline. It's circular combat. Circular warfare. So all of our soldiers that are in a combat zone are at risk for being killed or injured.

BY MR. SCHOETTES:

Q But not all of the soldiers have the same --

A Level.

Q Can I finish my question?

A Uh-huh.

Q Not all the soldiers have the same problems with logistics of supplies in the entire combat zone, do they?

MS. BERMAN: Objection. Vague and outside the scope.

You can answer, if you know.

THE WITNESS: I don't do supply -- I can't answer that. I guess that's a changing dynamic. So I don't think -- I don't have the answer for you.

BY MR. SCHOETTES:

Q Okay. Although it is in the opinion from Colonel Morgan that medication -- supply medications is a concern, correct?

A Of course.

Q And I'm asking you if the concern is different for people who are in combat versus the

people who are in a combat zone but not necessarily in a forward position?

MS. BERMAN: Objection. Vague and outside the scope.

You can answer.

THE WITNESS: And I'm going to say that -- their -- it can be the same. There's -- there is no -- logistics into a combat zone is inherently difficult, no matter where it is.

BY MR. SCHOETTES:

Q You're saying it's just as difficult for people in forward positions as it is for people in the rear?

MS. BERMAN: Objection. Mischaracterizes the testimony.

Go ahead.

THE WITNESS: I would say it's probably more difficult if you are in a forward position.

BY MR. SCHOETTES:

Q And as a member of the JAG corps, how common would it be to be placed into a forward

2-30A and says they're not waived regardless of which standards are applied, correct?

A Correct.

Q And 2-30A, which is Page 17, that includes HIV with or without progressive disease or immunological deficiency?

A Correct.

MS. BERMAN: That's all that I had.

MR. SCHOETTES: We're good.

VIDEOGRAPHER: And off the record at 1326.

(Whereupon, at 1:27 p.m., the deposition of PAUL TUMMINELLO was concluded.)

* * * * *

CERTIFICATE OF REPORTER

I, KAREN LYNN JORGENSON, RPR, CSR, CCR the officer before whom the foregoing deposition was taken, do hereby certify that the witness whose testimony appears in the foregoing deposition was duly sworn by me; that the testimony of said witness was taken by me in stenotype and thereafter reduced to typewriting under my direction; that the said deposition is a true record of the testimony given by said witness; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this deposition was taken; and further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action

KAREN LYNN JORGENSON, RPR, CCR, CSR

Dated this 28th day of February, 2019.

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February 28, 2019

To: Ms. Berman

Case Name: Harrison, Nicholas, et al. v. Shanahan, Patrick, et al.

Veritext Reference Number: 3220571

Witness: LT. COL Paul Tumminello Deposition Date: 2/13/2019

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ASSIGNMENT REFERENCE NO: 3220571
CASE NAME: Harrison, Nicholas, et al. v. Shanahan, Patrick, et al.
DATE OF DEPOSITION: 2/13/2019
WITNESS' NAME: LT. COL Paul Tumminello
In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.
I have made no changes to the testimony as transcribed by the court reporter.

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Date LT. COL Paul Tumminello

Sworn to and subscribed before me, a Notary Public in and for the State and County, the referenced witness did personally appear and acknowledge that:

They have read the transcript;
They signed the foregoing Sworn Statement; and
Their execution of this Statement is of their free act and deed.

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DEPOSITION REVIEW
CERTIFICATION OF WITNESS

ASSIGNMENT REFERENCE NO: 3220571
CASE NAME: Harrison, Nicholas, et al. v. Shanahan, Patrick, et al.
DATE OF DEPOSITION: 2/13/2019
WITNESS' NAME: LT. COL Paul Tumminello
In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.
I have listed my changes on the attached Errata Sheet, listing page and line numbers as well as the reason(s) for the change(s).
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They have read the transcript;
They have listed all of their corrections in the appended Errata Sheet;
They signed the foregoing Sworn Statement; and
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ERRATA SHEET

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ASSIGNMENT NO: 2/13/2019

PAGE/LINE(S) / CHANGE /REASON

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Date LT. COL Paul Tumminello

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EXHIBIT 51

Transfusion-transmitted human T-lymphotropic virus Type I infection in a United States military emergency whole blood transfusion recipient in Afghanistan, 2010

Shilpa Hakre, Mark M. Manak, Clinton K. Murray, Kenneth W. Davis, Meera Bose, Aaron J. Harding, Peter R. Maas, Linda L. Jagodzinski, Jerome H. Kim, Nelson L. Michael, Francisco J. Rentas, Sheila A. Peel, Paul T. Scott, and Sodsai Tovanabutra

BACKGROUND: The United States introduced human T-lymphotropic virus Type I (HTLV-I) screening of blood donors in 1988. The US military uses freshly collected blood products for life-threatening injuries when available stored blood components in theater have been exhausted or when these components are unsuccessful for resuscitation. These donors are screened after donation by the Department of Defense (DoD) retrospective testing program. All recipients of blood collected in combat are tested according to policy soon after and at 3, 6, and 12 months after transfusion.

CASE REPORT: A 31-year-old US Army soldier tested positive for HTLV-I 44 days after receipt of emergency blood transfusions for severe improvised explosive device blast injuries. One donor's unit tested HTLV-I positive on the DoD-mandated retrospective testing. Both the donor and the recipient tested reactive with enzyme immunoassay and supplemental confirmation by HTLV-I Western blot. The donor and recipient reported no major risk factors for HTLV-I. Phylogenetic analysis of HTLV-I sequences indicated Cosmopolitan subtype, Subgroup B infections. Comparison of long terminal repeat and *env* sequences revealed molecular genetic linkage of the viruses from the donor and recipient.

CONCLUSION: This case is the first report of transfusion transmission of HTLV-I in the US military during combat operations. The emergency fresh whole blood policy enabled both the donor and the recipient to be notified of their HTLV-I infection. While difficult in combat, predonation screening of potential emergency blood donors with Food and Drug Administration–mandated infectious disease testing as stated by the DoD Health Affairs policy should be the goal of every facility engaged with emergency blood collection in theater.

Human T-lymphotropic virus Type I (HTLV-I) is an intracellular human RNA retrovirus that is associated primarily with adult T-cell leukemia in 2% to 5% and HTLV-I–associated myelopathy or tropical spastic paraparesis in 1% to 2% of infected carriers.[1-3] Six subtypes have been identified: a (Cosmopolitan)—Japan; b to f—Central Africa; c—Melanesia; and e—South and Central Africa.[4-9] Isolates from West African countries are almost identical to those from the French West Indies, Haiti, French Guyana, and Peru.[8] While the genetic variability of the HTLV-I proviral sequence is relatively low when compared to other viruses such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV), epidemiologically linked infections

ABBREVIATIONS: ASBPO = Armed Services Blood Program Office; DoD = Department of Defense; FOB = forward operating base; IED = improvised explosive device; LTR = long terminal repeat; MTF(s) = military treatment facility(-ies).

From the Armed Services Blood Program Office, Falls Church, Virginia; the San Antonio Military Medical Center, San Antonio, Texas; the United States Military HIV Research Program, Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, Maryland; and the United States Military HIV Research Program, Walter Reed Army Institute of Research, Rockville, Maryland.

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The views expressed are those of the authors and should not be construed to represent the positions of the US Department of Defense.

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TABLE 1. Countermeasures employed to reduce the risk of transfusion-transmitted viral infection from freshly collected blood products in the combat theater of operations

Countermeasure	HIV	HCV	HBV	HTLV-I/II
Periodic screening of the force	Every 2 years*			
Theater entrance screening	Within 120 days†			
Vaccination	NA*	NA*	Required‡	NA
Volunteer donor screening questionnaire	Yes	Yes	Yes	No§
Volunteer donor pools‖	Yes	Yes	Yes	Yes
Rapid test	Yes	Yes	Yes	NA

* Force screen policy 2001—current by service and component for active component; every 5 years for reserve component.
† Central Command (CENTCOM) theater entrance requirement for predeployment HIV testing within 120 days of deployment, as of December 2011 (MOD 11).
‡ Universal vaccination during initial entry training since 2001. Required to initiate vaccination prior to entry in to the CENTCOM combat theater of operations.
§ Not currently utilized; recommendation has been made to consider modification of the DoD donor screening questionnaire (DD572) and include questions pertaining to risk for HTLV-I/II infection.
‖ Volunteers at facilities with blood donation capacity are screened for HIV, HBV, HCV, HTLV-I/II, West Nile virus, and syphilis. Donors are admitted to the donor pool upon receipt of negative test results and rescreened every 90 days after readmission. At the time of donation, donated units are tested for HIV, HBV, and HCV with rapid diagnostic tests.

have been identified.[10-12] In HTLV-I–endemic areas such as southwestern Japan, the Caribbean, sub-Saharan Africa, South America, and parts of Iran, seroprevalence rates range from less than 5% to 10%.[13]Infection is lifelong with transmission of the virus primarily through breast milk, sexual contact, blood transfusion, or from sharing needles in intravenous drug use.

Reports of transfusion-transmitted HTLV-I in the United States have been infrequent with the last such report in 1989.[14] The United States initiated HTLV-I screening of blood donors in 1988[15] to prevent transmission of the virus from transfusion of blood products.[14,16] As a lifesaving measure when stored blood products have failed and when existing US Food and Drug Administration (FDA)-approved blood products have been exhausted or are unavailable, the US military uses freshly collected blood products during conflicts for combat casualty resuscitation.[17,18] Health Affairs policy guidelines for non–FDA-compliant emergency blood collection include, in order of preference, 1) blood donors screened for FDA-mandated transfusion-transmitted pathogens within 90 days by a Clinical Laboratory Improvement Amendments–certified laboratory; military treatment facilities (MTFs) and US Naval vessels conducting predonation screening are required to maintain up-to-date rosters of eligible blood donors; 2) donors who self-report to have been nondeferred repeat donors; and 3) donors who neither have been screened for FDA-mandated transfusion transmitted pathogens nor have a history of donation.[19] The US military utilizes several countermeasures to reduce the risk of transfusion-transmitted viral infections from battlefield transfusion of emergency blood products collected in the deployed setting. Any MTF in the combat theater of operations with blood donation capability may initiate a walking donor program, which includes screening volunteers for HIV, hepatitis B virus (HBV), HCV, HTLV, West Nile virus, and syphilis. MTFs send samples collected from volunteers to a commercial laboratory in the continental United States for testing. After being tested, volunteers who screened negative are eligible to donate for a period of 90 days and are retested at 90-day intervals and at each donation event. Other countermeasures include universal HBV immunization and, in accordance with Health Affairs policy, screening of blood products for HIV, HBV, and HCV with rapid diagnostic test devices at the time of collection from donors in emergency situations who have not been screened in the combat theater of operations (Table 1). We report here the results of an investigation conducted as a result of the Department of Defense (DoD) retrospective testing program of non–FDA-compliant fresh whole blood.

CASE REPORT

The recipient, a 31-year-old US Army soldier, received 13 units of fresh whole blood in Jalalabad, Afghanistan, on the day of his injury after an improvised explosive device (IED) blast (Table 2). The soldier had sustained multiple injuries to the head, chest, midsection, groin, and lower extremities requiring chest tubes, fasciotomies, and washouts. Before arrival at the forward operating base (FOB) he had received basic care in the field on the day of the blast (Day 0, Table 2). He was transferred to Bagram Airfield from the FOB for a laparoscopic splenectomy and follow-up care, which included more washouts, external fixation placements, and splinting for his groin and fracture injuries. He received 4 units of platelets (PLTs). He was evacuated subsequently to a military hospital in Germany on Day 3 where he remained for 2 days for stabilization due to his traumatic brain injury, which required bolts for subarachnoid injuries.

On Day 5 he was transferred by a Critical Care Air Transport Team to a tertiary care military hospital in Texas where he remained for approximately 3 months before

TABLE 2. Timeline of events and testing for a lookback investigation of a donated unit which tested positive for HTLV-I, Afghanistan, 2010

Donor	Day	Recipient
1 unit donated in theater	0	IED blast; field medical care; 13 units fresh whole blood transfused, FOB Fenty, Jalalabad, Afghanistan
	2	4 units PLTs, BAF, Bagram, Afghanistan
	3	Medical evacuation to Germany
	4	Germany
	5	Transfer to a military hospital in United States for definitive care
Donated unit tested HTLV+	12	
	15	Lookback Test 1 = HTLV-I indeterminate
Notified in theater of HTLV diagnosis	31	
	44	Lookback Test 2 = HTLV-I ; notification and counseling
	180	Lookback Test 3 = HTLV-I+
	234	Reposed sample collected 142 days before transfusion = HTLV–
Reposed sample collected 265 days before donation = HTLV+	279	
	293	Epidemiologic interview; sample collection for HTLV sequencing
Epidemiologic interview; sample collection for HTLV sequencing	309	

BAF = Bagram Airfield.

being released to the Veterans Administration health system for follow-up care. While in care at the military hospital in 2012, recurring fever and increasing white blood cell counts in the soldier 29 days into his admission led to an infectious disease work-up for malaria, brucellosis, cytomegalovirus, Epstein Barr virus, *Clostridium difficile,* and Q fever. These tests, along with routine evaluation for nosocomial and other trauma-related wound infections, were unrevealing. In the midst of his infectious disease work-up, his providers received notification that the soldier's posttransfusion surveillance sample, drawn 19 days after the IED blast as part of the DoD retrospective testing program, had tested HTLV-I indeterminate: rg46-1 and -2 reactive, p19 and GD21 nonreactive (Day 19, Table 3). The sample had tested negative for HIV, HBV, HCV, and other pathogens. Retrospective testing performed 44 days after transfusion (Quest Laboratories, Irving, TX) indicated that the recipient had seroconverted and was HTLV-I infected: rgp 46-1, p19, GD21 reactive (Day 44, Table 3).

The Armed Services Blood Program Office (ASBPO) initiated a lookback investigation for the donors of the recipient. Mandatory testing of donation aliquots shipped to the United States after fresh whole blood combat theater donations had revealed a blood unit, donated 12 days prior in Afghanistan (Day 0, Table 2), that was positive for HTLV but negative for HIV, HBV, HCV, and syphilis.[19,20] The other 12 of 13 fresh whole blood units the recipient had received at the FOB had tested negative for HTLV and other blood-borne pathogens.

The ASBPO initiated another investigation to determine the HTLV-I infection status of the recipient and donor before transfusion and donation, respectively. The method has been previously described.[21] Briefly, the recipient's pretransfusion and donor's predonation reposed sera, residual sample from mandatory HIV force

TABLE 3. Results for donor and recipient samples tested in the lookback investigation of an HTLV-I–positive donated unit in Afghanistan, 2010

	Days in relation to donation/transfusion					
	Donor		Recipient			
Assay	–265*	128	–142*	19	44	180
HTLV-I/II EIA	R	R	NR			R
Western blot†						
Band interpretation				Ind	P	
P19				NR	R	
P24				NR	R	
GP46				NR	NR	
P26				NR	R	
GD21				NR	R	
P28				NR	R	
P32				NR	R	
RG46-1				R	R	
RG46-2				R	NR	
P53				NR	NR	
P36				NR	R	
Line immunoassay						
Interpretation	P	P				P
Streptavidin	NR	NR				NR
P19 I/II	R	R				R
P24	R	R				R
GP46	R	R				R
GP21	R	R				R
P19	R	R				R
GP46 I	R	R				R
GP46 II	NR	NR				NR

* Predonation and pretransfusion testing for donor and recipient, respectively.
† Positive for HTLV-I if P19, GD21, and RG46-I are reactive; positive for HTLV-II if P24, GD21, and RG46-II are reactive; indeterminate if criteria for positivity are not met; negative if HTLV bands are not present.
Ind = indeterminate; NR = nonreactive; P = positive; R = reactive.

testing, were retrieved from the DoD Serum Repository and sent to Quest Laboratories for HTLV testing (Days –142 and –265, respectively; Table 3).[22] For the donor, both a predonation sample, drawn 265 days before donation, and a postdonation sample, drawn 128 days after donation, were HTLV enzyme immunoassay (EIA) reactive and HTLV line immunoassay positive. The recipient's pretransfusion sample, drawn 142 days previously, was HTLV EIA nonreactive (Table 3). Since all evidence pointed to a case of transfusion-transmitted HTLV-I infection, an epidemiologic investigation was launched.

An infectious disease clinician interviewed both the donor and the recipient for HTLV risk factors using a standardized case report form for transfusion-transmitted viral infections. The interview indicated that the recipient was white and US-born and had served 13 years in the US military at the time of his transfusion. At the time of the interview, he had no signs or symptoms of HTLV-I/II: skin lesions; numbness, stiffness, or weakness of the legs; difficulty walking; acute bronchitis; asthma; pneumonia; leukemia; arthritis; abscess; lymphadenopathy; bladder or kidney infection; and *Staphylococcus* or *Strongyloides* infections. There was no evidence of HTLV infection–related neurologic disease on physical examination. The only risk factors reported were blood transfusions received in theater reported here, ear piercings, and corrective surgeries as described above for injuries sustained in combat. The recipient revealed no history of: sexually transmitted diseases, sex with a commercial sex worker, or injection drug user; incarceration; residence in a group or halfway home; tattoos; rape; needlestick; blood splash to mucous membranes; organ, tissue, or marrow transplant; and sex or household contact with a person with hepatitis, HIV, or HTLV-I/II or a person who had received clotting factors. He recounted that he had traveled to Australia, France, and Germany.

The donor was a US-born 32-year-old white male from the Pacific Northwest region whose parents were white and not of mixed race. He was an Army Reservist who had been in service for 3 years at the time of his donation. He reported having no awareness of HTLV infection until he was informed of his donated unit's screening results (Table 2). At the time of his interview, he reported no signs or symptoms of his HTLV-I infection and revealed no risk factors other than acquiring a couple of tattoos at reputable facilities and having had surgery as a child. He indicated no history of blood transfusions and denied having sex or household contact with a person known to have HTLV-I/II infection and did not report having sex partners from HTLV-endemic regions of the world. His travel history included trips to Germany, Prague, Poland, Spain, and Amsterdam.

Molecular characterization of HTLV-I from both the donor and the recipient was initiated to determine whether HTLV-I infection in the recipient was transfusion

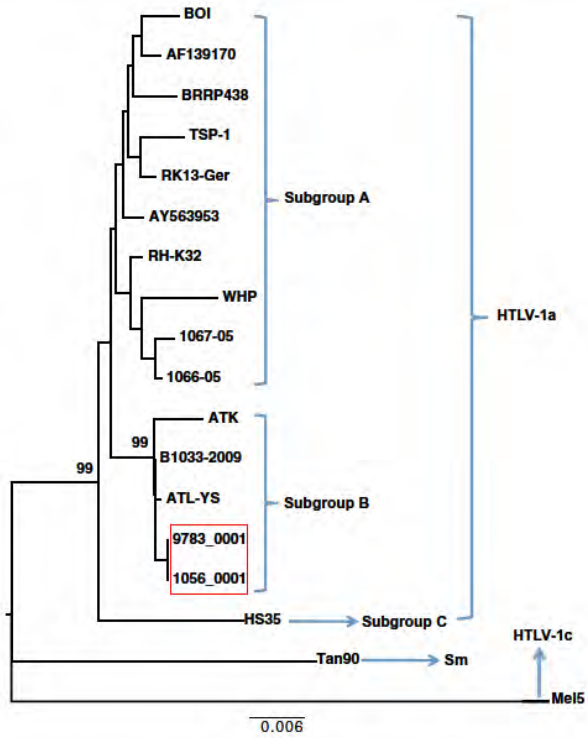

Fig. 1. A phylogenetic tree of HTLV-1 sequences from the donor (9783) and recipient (1056), as highlighted by the red box, and 16 HTLV-I subtype reference sequences was constructed by the maximum likelihood method using MEGA 5.05 software. The sequences were concatenated from 1353 nucleotides in envelope gene corresponding to ATK1 numbering Positions 5217 to 6569 and 433 nucleotides in LTR region corresponding to ATK1 numbering positions 8269 to 8700. The scale bar indicates the number of nucleotide substitutions per site estimated by general time reversible model with number of bootstrap replications at 1000.

transmitted. Blood samples provided at the time of interviews were sent to the US Military HIV Research Program for sequencing. DNA extracted from peripheral blood mononuclear cells was used for partial genome sequencing: 433 nucleotides of the long terminal repeat (LTR) region (ATK1 reference positions, 8269 to 8700) and 1353 nucleotides from the envelope (*env*) region (ATK1, 5217-6569). Phylogenetic analysis was performed using computer software (MEGA 5.05, http://www.megasoftware.net/). Due to the very low evolutionary rate of HTLV-1, a maximum likelihood approach with the number of nucleotide substitutions per site estimated by general time reversible model and number of bootstrap replications at 1000 was chosen for the analysis.

Maximum likelihood trees generated from LTR and *env* concatenated sequences (Fig. 1) showed that the virus sequences from the pair, 1056_001 (recipient) and

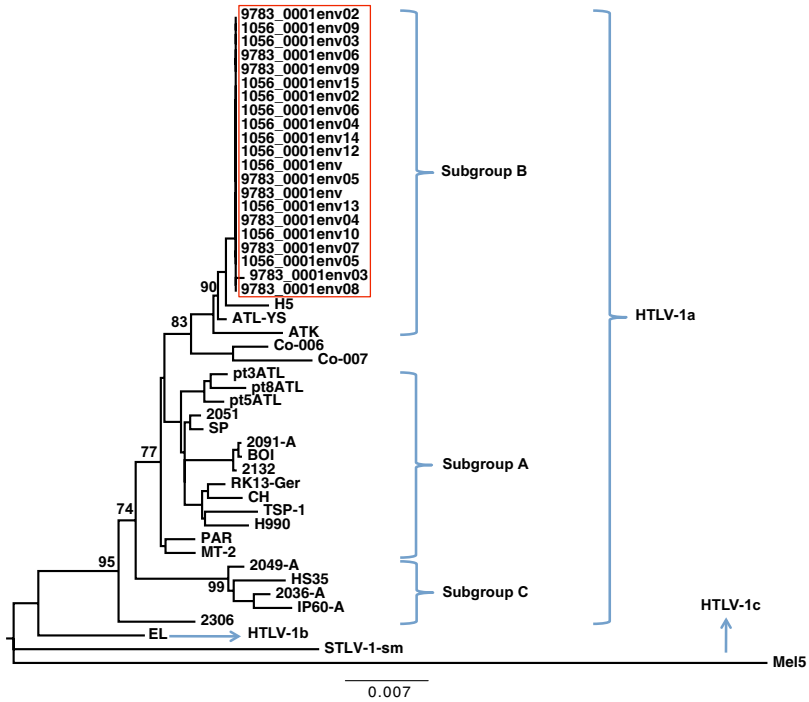

Fig. 2. A phylogenetic tree of HTLV-1 envelope genes corresponding to ATK Positions 5217 to 6569 was constructed by the maximum likelihood method using MEGA 5.05 software. There are 27 HTLV-1 subtype references and 21 envelope sequences from the donor (9783) and recipient (1056), as highlighted by the red box. The scale bar indicates the number of nucleotide substitutions per site estimated by general time reversible model with number of bootstrap replications at 1000.

9783_0001 (donor) clustered together with HTLV-I reference strains: Cosmopolitan subtype or Subtype a, Subgroup B (Japanese). To further confirm molecular genetic linkages between HTLV-I viruses from the donor and recipient, an independent polymerase chain reaction amplification reaction strategy was utilized. A DNA template at near endpoint dilution was used to generate an additional eight and 11 *env* gene sequences from the donor (9783) and recipient (1056), respectively. Comparison of these *env* sequences revealed nearly 100% sequence identity, except for a single-base pair (9783-0001*env*03) G-to-A transition. A maximum likelihood tree of the *env* sequences provided further evidence of a molecular genetic linkage between the viruses from these two individuals (Fig. 2).

DISCUSSION

We present a case report wherein evidence indicates that a service member was infected with HTLV-I after transfusion of non–FDA-licensed fresh whole blood. This transfusion-transmitted HTLV case is the first such report in the US military and a rarely reported occurrence in the United States; the last documented transmission in the United States occurred more than a decade ago but not since universal donor screening.[14,23] Transfusion-transmitted HTLV is strongly suggested for several reasons: 1) The recipient's pretransfusion reposed sample indicated no evidence of HTLV-I, whereas the donor's predonation reposed sample demonstrated HTLV-I infection; 2) the timing of the recipient's anti-HTLV status was consistent with a new infection: EIA positivity and indeterminate Western blot profile on Day 19 after transfusion, but full complement of HTLV-I bands by Day 44; 3) both the donor and the recipient were infected with HTLV-I Subtype a, Subgroup B; 4) viral sequences from the donor and recipient were nearly 100% homologous, indicating molecular genetic linkage; 5) the recipient had no major risk factors for HTLV-I; 6) clinical presentation of the recipient 29 days after transfusion fits the 30- to 90-day incubation period reported for HTLV before seroconversion.[24] The lookback investigation identified the donor who was unaware of his HTLV-I infection until notification of his test results in theater.

Prevention of transfusion transmission of HTLV in combat settings is challenging. While a voluntary HTLV screened donor pool is available near combat support hospitals and MTFs, in mass casualty scenarios, where prepositioned FDA-approved blood component supplies have been exhausted, or at smaller outposts, limited screening of emergency blood donors is possible. In the 2010 incident described herein, although 13 screened blood donors of

groups O and A were standing by at the FOB, the IED blast injuries necessitated additional donors since 54 fresh whole blood units were required for the ensuing mass casualties. Emergency donors are called from among volunteers who might be members of the receiving in-theater MTF, the recipient's military unit, or other civilian workers on the base and are referred to as the "walking blood bank." Theater infrastructure precludes donor screening with a FDA-approved screening assay and a Western blot investigational assay. Furthermore, a HTLV rapid kit has not been licensed for point-of-care use and questionnaires used in theater to screen emergency blood donors do not inquire about HTLV-I/II infection.

Since the issuance of the FDA guidance in November 1988 to screen blood donors for HTLV antibodies, transmission of HTLV-I/II has decreased in the United States.[25] A prevalence of 0.11 per 10,000 donations was found among first-time and repeat male US donors at the American Red Cross in 2009.[25] HTLV-I seroprevalence among US blood donors has been associated with older age, female sex, black race, birthplace outside the United States, and positive HCV serology.[26] US military blood donation centers in the continental United States, Hawaii, Germany, and Japan have routinely screened donors for HTLV-I/II since universal donor screening began in the United States (ASBPO). In 2011, of 91,656 donated units, 81 were repeat reactive by EIA of which 1 unit was confirmed positive by Western blot for a seroprevalence rate of 0.001% (0.11 per 10,000 units), which is consistent with that seen in US first-time donors (ASBPO). Donor screening and deferral in the US military for HTLV are based on FDA's 1997 guidance.[27] Donors repeatedly reactive for licensed HTLV screening tests are deferred from donation and placed under surveillance; in the combat theater, any donor testing HLTV positive on an initial screen is deferred indefinitely from theater donations. These donors are indefinitely deferred if repeatedly reactive a second time using screening assays. Although military health care providers may at their discretion request supplemental Western blot confirmatory testing for repeat-reactive donors, this information is not relayed systematically to the deployed environment. Screened donor pools at FOBs would be the best course of action to prevent future cases of transfusion-transmitted HTLV.

While the HTLV seroprevalence among blood donors in the US military and the general US population is low, and HTLV survival in stored red blood cells is limited,[16] the threat of transfusion transmission of HTLV-I/II among fresh whole blood recipients in the combat theater remains. Additionally, the seroprevalence of HTLV-I among US military personnel is unknown. Whereas modification of the predonation screening questionnaire administered to emergency blood donors to include questions regarding HTLV-I/II infection may be helpful, this would not have deferred donation in this instance. However, the utility of modifying the DoD donor screening questionnaire (DD572) to include questions pertaining to risk for HTLV-I/II infection should be considered. Since no licensed confirmatory assay is currently available for blood establishments, the use of HTLV Western blot assays should be employed to confirm any EIA HTLV reactive or repeat-reactive donor samples. Rapid detection of HTLV-I/II for emergency blood donations would be beneficial to prevent transfusion transmissions.

SEQUENCE DATA

Sequences described here were submitted to GenBank and are available under Accession Numbers JX984801-JX984802 and JX885208-JX885228.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to **TRANSFUSION**.

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EXHIBIT 52

BEFORE THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

RICHARD ROE, ET AL.,	)	Civil Action No.
	)	1:18-cv-01565
Plaintiffs,	)	
	)	
v.	)	
	)	
PATRICK M. SHANAHAN, ET AL.,	)	
	)	
Defendants.	)	
NICHOLAS HARRISON, ET AL.,	)	Civil Action No.
	)	1:18-cv-00641
Plaintiffs,	)	
	)	
v.	)	
	)	
PATRICK M. SHANAHAN, ET AL.,	)	
	)	
Defendants.	)	

- - -

FRIDAY, May 3, 2019

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Deposition of SHEILA PEEL, PH.D., taken at the offices of Winston & Strawn, LLP, 1700 K Street NW, Washington, D.C., beginning at 9:35 a.m., before Nancy J. Martin, a Registered Merit Reporter, Certified Shorthand Reporter.

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I N D E X

E X H I B I T S

custody for specimen management, and shipment, which are standard practices. I have no knowledge of whether they have shipped to HDRL a sample from a deployed person. So I can't speak to that practice.

Q. And you can't speak to how the Navy goes about collecting those specimens?

A. No.

Q. What about for the Air Force? First of all, does your lab conduct HIV viral load testing for the Air Force?

A. Upon occasion, yes.

Q. On occasion?

A. On occasion, yes.

Q. But you don't have responsibility for all of it the way you do with the Navy and the Army?

A. Correct.

Q. Can you describe -- do you know any of the logistics for collecting specimens for HIV viral load testing in the Air Force?

A. No. Can we flip -- can I clarify something?

Q. Sure.

A. For your question about whether I know how

logistics are met, HDRL has specimen submitting guidelines whereupon a submitting entity, whoever they may be, must follow and be in compliance with for submitting a specimen for testing, and there are prescribed requirements and submission guidelines for the laboratory which must be met, and those -- if they're not, then those trigger a rejection or an interaction with the site to determine what may have occurred in the context of chain of custody.

We do not provide phlebotomy services. All samples are required at distant sites and submitted in accordance with our specimen submission guidelines.

Q. All right. Do you know if members of all components of the Army are required to have their viral load testing done at a -- at HDRL?

A. No.

Q. Is it possible that some members get their viral load testing conducted through private medical treatment facilities here in the United States?

A. Yes.

Q. Are all active duty members required to have their viral -- of the Army required to have their

helpful if we had a conversation about the submission guidelines and what I think you're trying to get at here.

If you're within the local, what we call "national capital region" and you can get your viral load test to us within 24 hours, then the tube can be sent to us if it's sent four to six hours to be processed, or it's processed overnight in a specific tube. It's processed, held overnight, and gets to the lab within 24 hours.

Otherwise, the specimen is processed at the site of collection, and it is then frozen and shipped to the laboratory. As to -- so the laboratory support continentally through the United States, a fairly broad number of major treatment facilities. There are only -- there are fewer local facilities within the national capital region. So I cannot give you a percentage. But you could acquire the specimen, send it over to us, and we will process it in real time. The vast majority of specimens are processed at the site of collection. The specimen is frozen, and then it's shipped on dry ice to the laboratory.

Q. Thank you. So let me now clarify because now I think I understand the distinction being drawn.

So when I say, "processing," I was referring to, I guess, maybe two different things; right?

A. Right.

Q. So when you're talking about processing, you're talking about the -- well, I'll ask you. What processing takes place on site before a specimen is frozen?

A. So in my -- in specimen processing from a laboratory's point of view is the phlebotomy, the chain of custody, accurately acquiring the sample to the original test tube from a patient with all of the qualifying associated data that is then sent to a processing laboratory where it is centrifuged, aliquoted into a secondary container, essentially a cryotube --

Q. I missed the word that you used there.

A. The primary --

Q. Aliquoted?

A. Right. So viral load testing is very precise. It requires separation of the plasma

component of the blood in a very rigorous manner, and in the context of taking an EDTA anticoagulated tube of blood, a very specific anticoagulant that has been verified over time, whereby that tube is spun in a very narrow parameter for a specific period of time at a very prescribed rate.

And the reason is one must pellet the red cell component and one must remove the white cell component, what is called the "buffy coat" in the blood compartment. And you remove the plasma component with rigorous separation, and no contamination of the white cell or buffy component because what we are measuring is the burden of virus in the plasma. We do not want any contaminating virus cell, associated virus, from the buffy coat, which will artificially and inappropriately potentially elevate the viral load.

So that rigor is very prescribed. The specimen processing guidelines for the laboratory actually prescribe how that has to be done, at what rate, for what time, how long you leave the tube before you spin it, et cetera.

So all of that SOP, standard operating procedure, is made available to our clients so they understand the rigor that must be imposed. And if they cannot hand off that tube within a 24-hour period, it must immediately go into the refrigerator. If it can't be handed off in a 24-hour period, it, should be frozen and shipped to the laboratory frozen.

Q. So just so I don't forget to ask, the buffy coat, is that both the red blood cell pelleted and the white blood cells?

A. No. If we had a picture in our mind of a tube of blood that is red, it's whole blood, and then we spin it for 20 minutes, 1,600 times G. So but if we provide -- and I would have to go and look for -- it depends on what assay you're using and how long you do it. So don't pay attention to the numbers. Let's say now we pulled the tube out of the centrifuge and we hold it up. We have a yellow plasma component, and then we have band of white flocculent material. Those are your white cells. All right? Those which are measuring an immunopheno typing and what have you.

And below that is a red cell component. So

do you intend to testify regarding clinical testing relating to the detection or monitoring of HIV including equipment and procedures used by the U.S. military HIV research program to conduct HIV viral load and HIV genotype testing for clinical and therapeutic monitoring of U.S. service members beyond that to which you have already?

MS. CUTRI-KOHART: Objection. Compound.

But answer as best you can.

THE WITNESS: It is my understanding and I'm going to give testimony not only to how we conduct the testing, for our genotype monitoring, but in the context of a deployed setting of how that might be done or not done.

BY MR. SCHOETTES:

Q. All right. Let's -- we'll switch to something else. In your disclosure -- we're back to this.

In your disclosure, you indicate that it is your opinion that deployed environments present substantial medical and logistical challenges to conducting HIV viral load and HIV genotype testing for

deployed service members? Is that an opinion you will be presenting as testimony in this matter?

A. Yes.

Q. What are the medical challenges that you're describing there?

A. In the context of the current Army's readiness and battle space, the programmatic approach is to push small expeditionary forces far forward without the corresponding fixed medical assets that in previous areas of operation have been used. And in that context, when you are trying to medically manage individuals, you have to either use doctors and laboratories to patients, soldiers, service members -- or service members to doctors and laboratories.

And in open area of conflict, that's a very hard thing to do. Our management of our sets and kits are contact specific for the area of operation where they are used in an area in which they're deployed, and I'm not an expert on that. And in that context you can't be assured, but you'll have the right people, the right equipment, and the right supplies to manage this monitoring. I'll give you an example.

About a month ago I got a call from down range from Afghanistan seeking to know whether I thought an individual should be sent forward for further testing. The person was a detached individual who had actually donated blood and was reactive, and my laboratory team spent quite a bit of time trying to figure out how we might move the requisite supplies to the requisite people to get blood specimen acquired, processed appropriately, and shipped out the theatre.

So the -- and that's just for looking at someone who is trying to determine whether someone may be in an open area of conflict who may be HIV infected and simply getting a test back for that sort of testing scenario. Trying to manage shipment of test, particularly plasma for viral load and HIV resistance genotyping orders of magnitude are more complex. You need to be processing these sample as in real time. You need to be -- which means you need the equipment we've talked about previously. You need access to cold chain to manage the specimen and to freeze them, to then ship them out on a timely basis, which may require shipping to, say, Lackland Air Force Base in

the states or to Germany, but these are logistically constrained processes that are very, very difficult to manage in real time.

Q. So going back to the beginning of what you said about the newer approach of sending small expeditionary forces forward and the challenges of providing medical care in that setting, that would be across the board for medical care; correct? That's not specific to HIV related care?

A. No, that's true.

Q. What would -- so are medical treatment facilities described by different levels?

A. Yes.

Q. What level facility would be traveling with the small expeditionary force that you described?

A. I don't think that's in my lane to actually say because it's going to depend on what group is moving where and doing what.

Q. What's the lowest level of medical treatment facility that would be accompanying a force such as this?

MS. CUTRI-KOHART: Objection. Scope.

Go ahead and answer.

THE WITNESS: Well, there are special -- or SOCOM or special operations command forces that may have a medic.

BY MR. SCHOETTES:

Q. So that would not even be considered a Level 1 medical treatment capability?

A. No.

Q. What is the -- are special forces the only ones that would potentially only have a medic?

MS. CUTRI-KOHART: Objection. Scope.

THE WITNESS: That is out of my area of expertise to comment.

BY MR. SCHOETTES:

Q. But you are providing an opinion regarding the capabilities or the challenges presented by attempting to do viral load testing for soldiers who are deployed into various settings; is that correct?

A. That is correct, and it's based on the experience of talking to physicians and health providers down range who are seeking support trying to determine whether a person is HIV infected or not. It

has taken quite a bit of interaction on the part of my laboratorian managers who are laboratorian officers in the United States military, engagement with their colleagues down range to try to figure out how to acquire, process, and ship specimens just for that activity alone.

Q. I'll come back to that.

In order to decide -- or to render an opinion as to how difficult it would be to provide this type of testing, don't you need to know the capabilities of the medical treatment facilities that would be asked to provide this testing?

A. Certainly. And in the context of conversations with physicians, I ask questions about their capabilities. Role 1s don't have centrifuges. Role 2s may or may not. They may or may not have wet ice. They most likely will not have dry ice. It is situational dependent.

Q. So is there a level of medical care between -- that's provided to a particular unit between just a medic and having a role 1 medical treatment facility?

A. I simply said that the test -- the initial screening test that was conducted, the transmission of the transfusion medicine screen had a high false-positive rate and that I was -- the laboratory stood ready to support if the doctor chose to pursue testing.

Q. And did the doctor choose to pursue testing?

A. He did not.

Q. So you did not end up needing to collect the specimen for HIV testing?

A. That's correct.

Q. However, you were presented with some challenges when you were contemplating how you would do that. Is that my understanding?

A. That is correct.

Q. Was this individual situated with a role 1 medical treatment facility?

A. I do not know where the individual was situated. I know that the data relayed was that they were not readily available. I don't know situationally.

Q. So that the role 1 treatment facility was not

readily available. Is that what you're saying?

A. I do not know where the service member was located. I -- the indication was that this person was not currently where the provider was. I have no idea where their location was.

Q. As compared to the provider?

A. Who had contacted me.

Q. Let's talk about exactly what is needed to conduct the blood draw and -- well, let's just start there. What is needed to conduct a blood draw for HIV viral load testing?

A. You would need a tourniquet, a Vacutainer, sleeve, a needle, a blood tube, and an EDTA blood tube. You would need a centrifuge. You would need --

Q. Let me stop you there because, actually, my question was what is needed to conduct the blood draw.

A. Right.

Q. So that would end at the EDTA blood tube?

A. And a phlebotomist who's qualified to draw the blood.

Q. What is needed to process -- hold on.

What would then be needed in the next step to

process that specimen that was drawn?

A. All right. We'd also have to assume we have a marker that can mark the tube.

Q. Okay.

A. So we would need a centrifuge. So we would have to have a power supply. We would have a centrifuge. Secondary tubes to aliquot plasma into. We would need readily available cold chain or an ambient temperature control of 18 to 25 C. Cold chain of 2 to 8 C. A means to get the sample from where it was acquired under cold chain.

Q. Hold on. Let's stop again. Let's get sort of the part about the processing which requires a centrifuge, did you say?

A. Power supply.

Q. Let me ask my question.

So are there different types of centrifuges? Would it need to be a centrifuge of a particular level?

A. It would be a centrifuge capable of separating blood components.

Q. Okay. Secondary tubes for aliquot, you said;

right?

A. Pipet tips.

Q. I'm sorry?

A. We're not going to pour it. So we're going to have a relative. We're going to put it in a centrifuge. We're going to pull it out. We're going to have to have a means to transfer the plasma from the original tube that's been spun into the secondary tube. So that's going to be pipeters and pipet tips.

REPORTER MARTIN: P-i-p-e-t?

THE WITNESS: Yes, ma'am.

BY MR. SCHOETTES:

Q. So let me ask so it would need to be ambient temperature control of between 18 and 25 degrees Celsius. And then by when would you need, if you had temperature control at 18 to 25 degrees Celsius, how long would it be before you needed to have cold chain capability?

A. For viral load testing, you would want it as soon as possible. So you would want to put it at 2 to 8 degrees C, and then immediately freeze it.

Q. How long can it remain at ambient temperature

before being placed in the centrifuge?

A. It shouldn't be no more than four to six hours.

Q. And just so I understand, I think I understand, but I want to make sure. Cold chain just means being able to maintain a cold temperature for the specimen?

A. Right.

Q. Now let's talk about where it goes from there in terms of where it needs to be transported and by when.

A. Well, it depends on where it's acquired. If there is wet ice available, then you could transport it to a level facility that could freeze it, and then from there it could be transported out of the area. It's going to be where this individual is relative to the laboratory support and capability of where the individual is or where the individual is moved to. So you either move the individual to the laboratory support area or you have to do the best you can for it.

Q. So if you can keep it between 2 and 8 degrees

Celsius -- new question.

Does wet ice keep it at between 2 and 8 degrees Celsius?

A. It's zero roughly degrees. It's frozen. So it's technically slushy zero degrees.

Q. Okay. So wet ice takes it to the place where the specimen is frozen?

A. Exactly.

Q. And how long would you have before you needed to take it from the 2 to 8 degrees to being frozen?

A. You know, the truth of the matter is I think we would have to -- I'm an evidence-based person. I don't know the answer to that because I could tell you that I require that it be spun, separated, aliquoted and frozen in the states, and I would -- because I am evidence based, I don't know.

Q. Do you know if that evidence base exists? I understand that for purposes of your laboratory and the way you handle specimens in the United States that it is ideal -- or you require that they be aliquoted and then frozen, but do you know if the evidence exists to describe what the window period is before it

A. You would have to use charged liquid nitrogen transport. But I have no idea. We would not have access. I cannot imagine liquid nitrogen in theater.

Q. Got it. So dry ice really becomes the only option in theater for shipping of the specimen like that?

A. As far as I know, yes.

Q. When I refer to a level 3 medical treatment facility, do you know to what I'm referring?

A. It's probably Landstuhl, Germany, level 3.

Q. Do you know if there are level 3 medical facilities in the middle east?

A. I can't answer that. I don't know.

Q. Do you know what kind of equipment a medical treatment facility in the middle east has -- let me go back.

At a treatment facility in the middle east, a medical treatment facility of the military that is at the highest level available, do you know if it has a centrifuge?

A. I would be speculating. I have no idea. I know that we move sets and kits of medical equipment

to where we're operating, and it depends on the context of what we're doing and where we are, but I am not into medical logistics and I do not know what is available where.

Q. Okay. Do you know what's in the various sets and kits that you move to places where service members are deployed?

A. No. There may or may not be a centrifuge in a level 2. I do not know. It will depend entirely what that level 2 is being used for.

Q. Do you know how many level 2 facilities there are in CENTCOM?

A. No, I do not.

REPORTER MARTIN: In where?

THE WITNESS: C-E-N-T-C-O-M.

BY MR. SCHOETTES:

Q. Do you know how many level 1 treatment facilities there are in CENTCOM?

A. No.

Q. How is it that you're able to render opinion -- an opinion as to how substantial the challenges are with conducting HIV viral load testing

if you don't know what equipment is available in the deployed environment?

A. Because I have managed and consulted and engaged providers down range to acquire specimens for incident cases, and it has been an extraordinarily difficult endeavor. One case involved coordination with the Air Force to fly samples to Lackland Air Force base, which were then flown to Washington D.C., which were then couriered to my laboratory. It involved an enormous number of people to move a person to an area where a phlebotomy could occur and the sample was taken to a place where it could be centrifuged and aliquoted and then moved again to where it could be frozen and shipped, and then we had movement within the United States.

There have been individuals who could not be managed in theater who are actually extracted from theater and moved to Germany to Landstuhl, Germany. So it is -- over the course of our experience in the middle east, and particularly from 2003 forward, I have and my laboratory officers who are my lab managers have had to work with their peers in theater

to try to make this happen.

It has in no case been an easy or readily executed exercise. I have not yet had to do viral load or genotype testing, and those samples are critically important to be managed very well, with high integrity, cold chain managed, and we ensure their chain of custody.

Q. So are you saying that all of the -- all these instances that you're describing involved HIV screening and confirmatory testing?

A. Yes. There's a paper I think in Military Medicine from 2009 which I wrote with a colleague who called me, concerned they had had an acute respiratory -- acute retroviral syndrome case after rest -- R&R period. And we document how we got the samples out of theater, and I believe we may not have, but that interaction took a lot of moving parts and a lot of folks to get the samples to Walter Reed to test. It is not a trivial exercise.

Q. And the processes that you were describing are in the context of the current paradigm in which there are no soldiers with HIV deployed into CENTCOM?

specimen acquired and out of theater in a timely manner and preserved in the right way so that the testing had integrity.

Q. In part because it needed to be done relatively quickly?

A. Yes.

Q. Which might justify putting someone on a helicopter and sending them with the sample directly to the United States?

A. Well, probably not that far, but at least to a facility where it could be centrifuged.

Q. And they're not going to go in a helicopter to the United States.

A. Yes. Absolutely.

Q. You understand, however, that in the context of the potential of deploying soldiers with a fully expressed viral load that there would not be the same urgency in obtaining their viral load test results; correct?

A. It would depend on the context on why the test was being done.

Q. And in what context would it require greater

urgency?

A. There is a condition called compartmentalized virologic failure, and that is a mental status change where the physician is concerned that perhaps there's viral load in central spinal fluid -- cerebral spinal fluid, CSF, that at times it can happen -- it's rare but it does happen in individuals who have a suppressed blood compartment viral load. That would be certainly an urgent scenario.

Q. You said that's rare. How rare is that?

A. You would have to ask my medical colleagues. We do support that testing at HDRL, the lab we're talking about. In the context of managing an individual who perhaps have lost their medication, there would be a sense of urgency to conduct a viral load to ensure that they're still controlled.

Routine monitoring, I'm certainly not saying it couldn't be set up, but I'm not sure, and you'll have to talk to my colleagues who are medical logisticians who are responsible for moving sets and kits. It's my understanding that, as you add things, you must take things out because we have space and

weight constraints, and in that context how that's managed and what is needed which is not already there, if it were added, it is my understanding other things may have to come out.

And this is not my area of expertise, but it is -- it does constrain what the military can effect from the medical side of the house in the context of the trauma support, which is going to be the priority relative to something that's more routine. That can be quite constraining.

Q. So on the things on the list -- of the things on the list that we have created that are required for HIV blood draw, HIV testing blood draw and then initial processing, and then shipping, what items are unique to HIV testing? HIV viral load testing. Do you need a tube with a particular reagent in it to collect the blood into?

A. EDTA tubes are standard. Clinical centrifuges are standard at certain levels.

Q. The tubes for aliquoting, standard?

A. Not necessarily, no.

Q. Okay. So is that an item that is unique to

HIV viral load testing or those secondary tubes also used for other purposes?

A. I am not sure of the total range of test capability in theater. Generally what you are trying to do is spin a centrifuge down on a primary tube and then testing from that primary tube. You don't aliquot off normally. But it may or may not be there. Granted.

Q. And then the wet and the dry ice are both things that are commonly used for other specimens that might need shipping?

A. At a certain level of facility. Certainly not at lower-level facilities.

Q. The pipets and the pipet tips, are those commonly used in a healthcare setting?

A. Yes.

Q. So what is it that you're saying would need to be moved out of a kit or set in order to routinize HIV viral load testing?

A. I think the issue here is where is the individual.

Q. Actually, I want to go back and --

unique constraints that are actually imposed about where you're operating by just geographically about where you're operating and what's available.

MR. SCHOETTES: So just a few follow-up questions and we'll take our break, Rebecca.

Q. So my question was asked a little poorly. So I want to rephrase it and say what would need to be added to a set or kit in order to conduct HIV viral load testing? And I should say at the highest level of treatment facility in a particular area of responsibility.

A. You're going to need -- as I said, you're going to need phlebotomy supplies. You're going to need the capacity to process the specimen. You're going to need the capacity to manage the cold chain, freeze it, and you're going to need a readily available shipper to --

Q. My question was we went through the list, and there was nothing on this list that is unique except perhaps the secondary tubes for aliquoting, but that everything else were things it seems would be at a moderate level medical treatment facility.

A. You know, I think there are folks better than I to speak to what's available on a moderate level facility. What I have to support is globally deployed force. Moderate to higher-level facility in Iraq and Afghanistan is going to mean something entirely different than the Congo or the DR.

Q. So first I'll just say I kind of got into CENTCOM because of the examples you used were coming out of CENTCOM.

A. Understood.

Q. So that's why we were talking there. I guess it would be easiest if we were able to talk in level of facilities. If we were talking about a level 3 and a level 2, are you saying that level 3s are different from CENTCOM to Africa?

A. Yes. Level 2s are. That's -- the point is contextually there's standard kits and sets, as I understand it. As I keep saying, this is not my area of expertise, but we have -- I've used the level -- I've used CENTCOM as an example, and it has not been easy to acquire samples and get them with integrity out of CENTCOM. We have personnel that I've tried to

by a submitting entity when they submit specimens.

The only way if we are in violation of the requirement of the specimen, the specimen can be tested is if I, as a laboratory director, approve that test. So in case-by-case basis, yes, there are times when I will approve testing when we have not received samples that were as prescribed.

It is generally after conversation with the provider when I have had like an understanding of the complexity of the case and whether the samples can be reacquired. There are many mitigating circumstances. These are obviously guidelines. It says, "GUIDELINES." And my role as the lab director is to try to balance getting the provider the best result for his patient because one of the things that's really important to remember here is that there's a handshake of trust between the lab and the provider, and that is on behalf of the patient.

So I am pretty strict, but I'm not impossible. I will work with the provider in the context of the case and what is wrong with the specimen. Sometimes you just can't. It's cracked and

leaking all over the place, and you're done.

You know, there are other times when it's a maybe. The potential is that it will be a false negative result; right? And we, as a laboratory, work with the providers and DOD to try to ensure that we're testing with the highest integrity but in the best interest of the service member. So that's about the best I can do.

Q. No, that is helpful. You just said that the risk, of course, is that there would be a false negative, and that is for someone who is testing -- screening for HIV; correct?

A. Well, in any context of any test. You may not get -- you may -- not just HIV. It may be a false negative for any STI. It could be that the viral load comes out as 100, well as 100,000 because it got exposed to bad temperatures or something --

Q. So that was my question. I wanted to know -- and I think you just identified it -- what the risk is with respect to accepting a specimen that doesn't meet all the guidelines for conducting HIV viral load testing and you just identified one. Are there other

potential risks?

A. Well, we may not be able to do a genotype, for example, on a patient who actually has sufficient verenia but because of the exposure of the sample to conditions that rendered it incapable of being run, then you would not be providing the provider with the information they need.

Q. Right. I guess what I'm wondering is is it a matter of the test would not -- you would not get a result at all, or you would get a false result with respect to HIV viral load testing, let's say?

A. It could be either/or. It depends on what the sample's projectory was and how it was handled and what it was exposed to. In other words, how to get from the patient to us. That's called "chain of custody." If it's violated at any point, it could be exposed to conditions that don't generate an accurate result.

Q. So your confidence interval on that result drops?

A. Significantly, yes.

Q. How frequently are HIV positive members of

cannot perform testing on human specimens unless you are an accredited laboratory either as a clinical with a CLIA certificate at a minimum or a College of American Pathologist accreditation.

The Department of Defense has a memorandum of understanding with HHS, and its laboratories are not CLIA certificate but have CLIP certificates. The CLIP certificate is a Clinical Laboratory Improvement Program certificate which is associated with the clinical laboratories CAP certificate.

What that means is that every two years your clinical lab is inspected by a peer review team, which comes and uses an established set of checklists to evaluate your performance to deliver laboratory services with quality.

So I am, by regulation, the director of that laboratory, and I'm expected biannually and when that inspection occurs and we successfully pass that inspection, then the DOD renews my CLIP certificate. So this is not a research lab, even though I'm in a research institute. This is a clinical lab.

Q. There was also a little bit of discussion

about how you came to your opinions in the disclosure that's in Exhibit 2 here.

A. Uh-huh.

Q. Can you explain what parts of your experience form the basis for the opinions that you're offering in this?

A. I have been doing clinical laboratory and testing, particularly for thyroid and resistance genotyping since the inception of the assays for 1998 for viral load testing, and 2003 for resistance genotyping.

I have managed, since 2005, the movement of these specimens to ensure integrity of tests. I daily have conversations with healthcare providers throughout DOD who have interesting cases, difficult -- diagnostically difficult test scenarios, some down range, some continental United States and how we manage and move the specimens and ensure the integrity of the tests. I've been doing this now for 14 years.

Q. In terms of your opinions regarding the logistics in the employed environment, is at least

some portion of the opinions based on your personal experience in terms of logistics, getting samples out of the deployed area?

A. It is. It is challenging. As I noted, there's a publication for military medicine. I can't at this point -- and I think it was about 2009 or '10, the numbers of people and the effort it took to get specimens out of theater were extraordinary in terms of assuring cold chain, just getting the service member to the preventative medicine doc to ensure the exam, the acquisition of the specimens, the support of their transport appropriately.

As I said, it took -- it was actually on an Air Force flight which was carrying samples for transfusion medicine testing that went all the way to Lackland Air Force Base, which then had to come back to Washington, D.C. and then be couriered on. So this process has been -- every time we have engaged in this process -- it has not been that many times, but every time we have had to do so, it has taken many people dedicated in a very dedicated effort to get the samples where they needed to go with the highest

integrity possible.

Q. And during your testimony you talked about a recent occasion where you thought you were going to have to bring a sample back from Afghanistan. It turns out you didn't, but can you tell me what the plan was you had in place to bring that sample back?

A. We had a plan in place to move the individual from where they were to the provider to have blood drawn. There was then going to be a move to the facility that I don't know the name of to centrifuge, process the sample, move the sample on a flight that was going to be moving to Germany, and then the flight from Germany, they would have taken the sample and then forwarded it onto the lab, and I could tell you I get samples from Germany almost three times a week. It takes two days for samples to reach the lab. So there was a stepwise plan in place.

Q. Was that sample going to be frozen somewhere?

A. It would have been frozen. I don't know where it was going to be frozen. That had not yet been worked out yet. So...

Q. We talked a little bit about freezing samples

by packing them in dry ice. Once a sample is packed in dry ice, how long does that 2-pound packing last?

A. About a day. If you look at the specimen guidelines -- and this will clarify something I said earlier. I said 2 pounds of dry ice. What I didn't specify was it's 2 pounds of dry ice per day that you expect it to be shipped. So over a three day, 72 hours, you would need at least 6 pounds of dry ice, and we recommend about 10.

Q. What happens if a sample is defrosted?

A. It depends on what test you're doing. So there's a sensitivity scale for genetic material, which is the most sensitive for a false-negative test to protein to antibody. So if you are going to be conducting viral load or resistance genotype testing, you want samples that have not been thawed.

MS. CUTRI-KOHART: Okay. I'd like to introduce Exhibit 5.

(Deposition Exhibit 5 was marked for identification.)

BY MS. CUTRI-KOHART:

Q. Can you turn to page -- it's marked at the

Q. If you were directed to regularly support viral load testing in a combat theater, what logistics would you recommend putting in place?

A. All of the equipment that we spoke about in the context of a level that could process specimens. There would be -- there would need to be -- in the context of moving sample to lab, I would recommend putting a rigorous validated capability of cold chain, even if it were a small box, that could be moved over time that would have a 72 hour, 2 to 8 degree refrigeration stability so it could get, hopefully, to a facility where it could be processed, and the process would then have to have requisite dry ice and shipping capability.

We would also need to manage either out of theater on military transport, since in many cases commercial entities will not fly into active combat zones. We would have to develop a scenario where we had routine management of clinical specimens in such a manner that there was a chain of custody and the specimen or the package wouldn't get lost. And a developed pathway out of that area of responsibility

to a center that could forward it on, be it Korea, for PACOM, Germany, for CENTCOM.

I mean we would have to really set a structure in place where you're managing all the clinical requirements for instability and quality that are applied in the U.S. in such a way that when it got to the lab for testing, that we had confidence in the result.

BY MS. CUTRI-KOHART:

Q. Some of the things you're describing, would they require power?

A. They require power. They require the capability of generating dry ice or acquiring dry ice. They require some newer approaches to cold chain stability, and they certainly require hand-off with chain of custody where it moves through the system and can be tracked.

Q. Based on your experience, are these types of things already available in austere environments?

A. No.

Q. Now let's talk about what happens when the sample actually arrives in your lab for testing. Why

And then Zone 3 is where you have amplification and detection. So each of these zones are rigorously maintained. The flow is actually directional. 1 to 2 to 3 so that you don't go backwards from Zone 2, which is dirty into your clean reagent zone.

So those facilities take space because you have to manage the workflow of people, reagents and specimens.

Q. When the sample is received, how is it prepared for testing? What do you do to get it ready for testing?

A. If it is from a local hospital and it hasn't been spun, then we process it as I've described previously. We centrifuge it according to the standard operating procedure for that assay. We aliquot off the amount of specimen required for the test if we are going to run that day. It is then moved onto the run, or if it's going to be held over until the next day, the sample is aliquoted into a sterile cryotube and then frozen.

Q. When you receive a frozen sample, what do you

do to prepare it for testing?

A. We simply put it -- if we -- if it's come early enough and there's room on a run, we will move it into Zone 2 to thaw it, and then it will move through the test facility. If not, it will be accessioned, as I've described before, and placed into, I want to say a freezer, to wait for the next run.

Q. And you mentioned the run occurs on something called an analyzer. What type of analyzers are used in your lab?

A. So these are huge robotic platforms we use to manually extract all our samples.

This particular platform has an automated extraction platform, which is a very large X, Y, Z robotic system that does -- and it's called a closed system. It does -- it makes every pipetting action independently. It uses new plasticware for each step in the reaction. It has reagents that are timed and that are managed in closed containers such that there is no extraneous or potential for cross-contamination of samples.

And then, as I said, I don't have a docking station. So it doesn't move just on into the amplification detection. There is one point where the staff have to intervene. They remove the plate which has all the K tubes on it, which are capped for exposure and then moved onto the PCR platform.

Q. You said it was large. How large is it?

MR. SCHOETTES: Objection. Vague.

BY MS. CUTRI-KOHART:

Q. You said the analyzer was large. How large is the analyzer?

A. It's about 6 or 7 feet long. It's about 4 feet tall and about 2-1/2 to 3 feet wide. It has lines for buffers and waste and a computer to drive it. So it takes a small -- a 10 by -- the whole piece is in an 8 by 12 foot --

Q. And what does your lab do to maintain its analyzer?

A. It is maintained daily. It is maintained weekly. It is maintained monthly. It has two preventative maintenances a year by the contractor. This is a proprietary piece of equipment. So it must

be maintained by the manufacturer, essentially. The waste test has to be maintained and shipped out. That's picked up twice a week.

Q. Does it have a power requirement?

A. It has a dedicated power requirement. It must run 24-7. If it is turned off, it must be recalibrated.

Q. Does it use -- you mentioned it does use reagents in it?

A. Yes.

Q. Do those reagents have any storage requirements?

A. Those are 2 to 4 -- 2 to 8 degrees. Some of the controls have to be frozen. So yes. And there are some room temperature reagents that must be maintained between 18 and 25 C.

Q. Are there other options that are smaller, easier to maintain that you could use for this purpose?

A. Not at the present time.

Q. And then after the analyzer, the sample moves to a PCR machine; is that correct?

that are complimentary to the sequences. They bind. First, we heat the CDNA because remember, it's copy DNA bound to RNA. So we have a dual strand. Then we heat it very hot. We separate the strands. We lower the temperature. The primers anneal, and then we lower the temperature again -- or raise it slightly, excuse me.

And the base pairs that have been added, the polymerase that's in the enzyme that will actually make us DNA sequences puts in the appropriate complimentary base. It's actually a fabulously cool technology because you can take one double strand of DNA and amplify it to a million copies. So you really -- you know, whatever is present is amplified.

BY MS. CUTRI-KOHART:

Q. What does your lab do to maintain your PCR machine?

A. Oh, my goodness. It's like the buffers have to be washed every day. The lines have to be flushed every morning. The robot has to be maintained. It takes quite a lot of work.

Q. How large is the PCR machine?

A. Now that's only about 2-1/2 feet by a foot or so.

Q. Does the machine use any reagents -- the PCR machine use any reagents?

A. No. It's actually amplifying what's there relative, as I said, to the internal quality control, and then the software figures out how much there is in the context of -- you are -- as I said, you have input of quality, a QI standard which is a small fragment of genetic material which is amplified at the same time as the -- what is present relative to the amplification of the internal control versus what is amplified in the software does all of its magic, figures out what the level of the virus is in the sample.

Q. To your knowledge, does any of this equipment exist in theater?

A. No, not to my knowledge.

Q. What would it take to set up a viral load testing capability in theater?

A. It would be quite an effort. We would have to acquire the platform, validate it in place, train

personnel to use it. It's generally fairly specialized. It would be a considerable undertaking.

Q. Let's switch to resistance genotype testing. You've already talked quite a bit about it, but just to be clear, do you use the same sample for the resistance genotype testing as you do for viral load testing?

A. No.

Q. So you have to acquire a different sample, but it's acquired the same way?

A. It's acquired the same way.

Q. And it has the same cold chain requirements as the viral example?

A. It does.

Q. And the same preparation requirements --

A. Yes.

Q. Same temperature requirements?

A. Yes.

Q. Can you walk me through how a genotype test is performed, a resistance genotype test is performed in your lab?

A. So some of the steps are the same. You are

This is run on a capillary gel, negative to positive, which separates out from smallest to largest, and these fluorescent nucleotides are moving down a gel matrix that pass the laser, and the laser reads the signal and actually captures each base pair.

So then what the software does is take all of the seven primers and makes -- and the reads that have happened, if this makes any sense at all, it makes a consensus sequence. That consensus sequence from the patient sample is then compared to a standard which has no mutations. So what is presented is a chromatogram for each base, and where there is a mutation or a change from the non-mutated sequence, it demonstrates where the change is.

Q. So we've talked a lot about the chemistry of this. How many lab stations are used physically to get to that process?

A. Oh, my goodness. All right. So you have Zone 1, Processing Zone 2, CDNA synthesis, clean-up. We have to make the gel on a sequencer, sequencing reaction, sequencer, and a software analyst station. So eight or nine stations.

Q. In addition to the analyzer and the PCR machine, what other lab equipment is used?

A. Well, there are smaller PCR -- four small PCR platforms, a speed vac to clean up the reactions, dry them down. So the sequencer itself takes an entire room -- it takes about two, three, four, five rooms to do this. It takes five separate spaces to do this.

Q. Okay. What would it take to perform resistance genotype testing in theater?

A. I don't -- this is certainly a test that could not be done in theater. I mean the Army can do anything, we've acknowledged. We drop things out of the sky. I get that. But this would not be one that I would accept.

Q. Okay. We also haven't really talked about this, but there is also CD4 testing that is performed on HIV patients. What is CD4 testing?

A. While you are looking, as I talked about, so HIV is distributed throughout the body, but it is -- the CD4 T-cell is its resident home in the human body, and it is -- has been and early on it was a marker of the -- what should we say -- the competency of a

immuno suppressed patients, be they transplant patients or HIV patients. It's a routine test that's done.

Q. Does your lab perform CD4 tests?

A. Not anymore. Not anymore.

Q. Would it require a different sample to perform CD4 testing than what is used to perform viral load testing?

A. It takes whole blood, yes. It takes a different sample.

Q. Very last subject, are there -- jumping to a related subject. Are there any FDA approved point-of-care tests for viral load?

A. No. No, there are not. There are not.

MS. CUTRI-KOHART: That's all I have.

FURTHER EXAMINATION

BY MR. SCHOETTES:

Q. Just a few follow-up questions. You mentioned Germany in a previous answer. Are there labs in Germany that can conduct HIV viral load testing?

A. That's what we recommend, yes.
Q. And the question was asked how long would a package with 2 pounds of dry ice last, and I believe you gave the answer of one day; correct?
A. Yes, assuming it's not sitting in 120 degrees; right?
Q. Then it's also true that what's recommended per your guidelines is that enough dry ice be included to last three days; correct?
A. Yes. 6 pounds. Yes.
Q. And you recommend actually 10 pounds to give yourself a bit of cushion if it does end up in some 120-degree heat; correct?
A. Or if it gets stuck in Customs.
Q. Things happen; right?
A. Things happen. That's right.
Q. So you give yourself a little extra cushion of dry ice to ensure that it remains frozen?
A. Correct.
Q. Could the level of dry ice be increased to an amount that would give you five days of shipment plus some cushion?

A. Certainly.

Q. We talked before about the fact that it's harder to provide all kinds of care, medical care in a deployed environment; correct?

A. Uh-huh.

Q. In your discussion before, when you were asked questions by Rebecca, you talked about why the lab work for an HIV viral load in the Army is centralized, and it creates that idealized situation of you having good labs and consistent -- using consistent methods for all of your service members with HIV; correct?

A. Correct.

Q. But given that care in a deployed environment is sometimes not idealized, would it be possible to have a different labs conduct those occasional tests when an individual is in a deployed environment?

A. Yes.

Q. You spent quite a bit of time discussing the equipment required to conduct viral load testing and genotype resistance testing in your lab; correct? First of all, is there a different way of conducting

the experiences you've had in trying to transport specimens for HIV screening or viral load testing and again expressed the difficulties that you face in doing so. I just want to clarify that there were no formal processes in place to guide your decision making as to how to make -- conduct that testing -- I'm sorry -- to collect those samples and be able to conduct the testing at your lab?

MS. CUTRI-KOHART: Objection. Form and compound.

Go ahead and answer.

THE WITNESS: There was -- no. It was a different scenario in each case.

BY MR. SCHOETTES:

Q. And you were kind of figuring it out as you went?

A. As you go along.

MR. SCHOETTES: That's all I have.

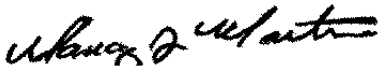
MS. CUTRI-KOHART: Okay. I don't have anything else.

(Witness excused.)

(Deposition concluded at 5:30 p.m.)

C E R T I F I C A T E

I do hereby certify that the aforesaid testimony was taken before me, pursuant to notice, at the time and place indicated; that said deponent was by me duly sworn to tell the truth, the whole truth, and nothing but the truth; that the testimony of said deponent was correctly recorded in machine shorthand by me and thereafter transcribed under my supervision with computer-aided transcription; that the deposition is a true and correct record of the testimony given by the witness; and that I am neither of counsel nor kin to any party in said action, nor interested in the outcome thereof.



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Nancy J. Martin, RMR, CSR

Dated: May 19, 2019

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ACKNOWLEDGMENT OF DEPONENT

I, SHEILA PEEL, PH.D., do hereby certify that I have read the foregoing pages, _____ to _____, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

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Subscribed and sworn to before me this _____ day of _____, 20__.

My commission expires: _____.

_____

Notary Public