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Update: Outbreak of Severe Acute Respiratory Syndrome — Worldwide, 2003

CDC and the World Health Organization (WHO) are continuing to investigate the multicountry outbreak of unexplained atypical pneumonia referred to as severe acute respiratory syndrome (SARS) (*1*). Pending development of confirmatory laboratory testing capacity, CDC's interim suspected SARS case definition (*2*) is based on clinical criteria and epidemiologic linkage to other SARS cases or areas with community transmission of SARS. This case definition will be updated periodically as new information becomes available. Epidemiologic and laboratory investigations of SARS are ongoing. As of April 2, 2003, a total of 2,223 suspected and/or probable SARS cases have been reported to WHO from 16 countries, including the United States (*3,4*). The reported SARS cases include 78 deaths (case-fatality proportion: 3.5%). This report summarizes SARS cases among U.S. residents and surveillance and prevention activities in the United States.

Descriptive Epidemiology

As of April 2, CDC had received 100 reports of suspected SARS cases (Figure) from 28 states; 81 (81%) cases occurred among adults (Table). Of these 100 suspected cases, 94 (94%) persons had traveled within the 10 days before illness onset to the areas listed in the case definition (revised on March 29 to include all of mainland China as an area with documented or suspected community transmission), four had household contact with a person with suspected SARS, and two were healthcare workers (HCWs) who provided medical care to a patient with suspected SARS. Manifestations of SARS have been relatively less severe among patients in the United States than among those reported elsewhere. A majority of U.S. patients had normal chest radiographs, and 23 (23%) were reported to have pneumonia or respiratory distress syndrome on chest radiograph, thereby meeting the WHO case definition of a probable case (*4*). As of April 2, of the 40 (40%) patients who were hospitalized for ≥24 hours, 13 (33%) remained hospitalized; one patient had required mechanical ventilatory support, and no deaths have been reported.

Reports on the clinical status of suspected SARS cases are being received by state health departments and CDC, and household and HCW contacts are being monitored for the possibility of secondary transmission. Since SARS investigations in the United States began, some persons believed initially to have suspected SARS have been excluded on the basis of more complete clinical histories (e.g., no documented fever or respiratory symptoms) or because of testing results that indicated other etiologies. Alternative diagnoses have included infection with influenza virus, respiratory syncytial virus, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus*. Community transmission of SARS has not been identified in the United States; transmission to HCWs has been observed in one cluster involving two HCWs, compared with numerous reports of possible transmission to HCWs in other countries (*5–7*).

INSIDE

Hepatitis C Virus Transmission from an Antibody-Negative Organ and Tissue Donor — United States, 2000–2002

In June 2002, a physician reported to the Oregon Department of Human Services (DHS) a case of acute hepatitis C in a patient who had received a patellar tendon with bone allograft from a donor approximately 6 weeks before onset of illness. At the time of the donor's death in October 2000, his serum had no detectable antibody to hepatitis C virus (anti-HCV). The ensuing investigation conducted by CDC and DHS confirmed that the donor, although anti-HCV–negative, was HCV RNA–positive and the probable source of HCV infection for at least eight organ and tissue recipients. This report summarizes the preliminary results of the investigation. Although transmission from anti-HCV–negative tissue donors probably is rare, determining the frequency of transplantations from such donors and the risk for transmitting HCV to recipients is important in evaluating whether additional prevention measures are warranted.

The donor was a man in his 40s with a history of hypertension and heavy alcohol use who died of an intracranial hemorrhage. At the time of death, he had no signs or symptoms of hepatitis, and his alanine aminotransferase and aspartate aminotransferase levels were normal. Physical examination revealed no skin markings indicative of injection-drug use or evidence of liver disease. A questionnaire administered to the donor's next of kin revealed no history of injection-drug use or blood transfusion.

At the time of the donor's death, his serum tested negative for anti-HCV by a second-generation enzyme immunoassay (EIA) (Abbott HCV EIA 2.0, Abbott Laboratories, Abbott Park, Illinois) and negative for human immunodeficiency virus (HIV)-1, HIV-2, human T-lymphotropic virus (HTLV) I, HTLV II, hepatitis B virus, and syphilis. In July 2002, stored, frozen serum obtained premortem from the donor tested negative for anti-HCV with a third-generation EIA (ORTHO® HCV Version 3.0 ELISA, Ortho-Clinical Diagnostics, Raritan, New Jersey) but positive for HCV RNA (AMPLICOR® HCV Test, version 2.0, Roche Molecular Systems, Branchburg, New Jersey). The donor's HCV genotype was 1a, as determined from the 300-nucleotide sequence of the nonstructural coding region NS5b (*1,2*).

A case was defined as laboratory-confirmed HCV infection, with a viral genotype identical to that of the donor, in a recipient not known to have been infected before transplantation. A definite case was defined as one that occurred in a recipient who was both anti-HCV– and HCV RNA–negative before transplantation. A probable case was defined as one that occurred in a recipient for whom no serum was available before transplantation.

The organ procurement and tissue distribution agencies provided an inventory of grafts recovered from the donor and the contact information for each health-care provider or facility that had received grafts. Health-care providers were contacted to obtain clinical information and to arrange for testing of recipients. Recipients' post-transplantation and stored pretransplantation sera, when available, were tested for anti-HCV by EIA 2.0 or 3.0 and for HCV RNA (by using either AMPLICOR® HCV Test, version 2.0, or HCV RNA DetectR™ PLUS by TMA, Specialty Laboratories, Santa Monica, California). Specimens positive for anti-HCV by EIA were tested with a supplemental recombinant immunoblot assay (RIBA®, Chiron Corporation, Emeryville, California). HCV genotype was determined for all HCV RNA–positive samples (*1,2*).

Of 91 organs and tissues recovered from the donor, 44 were transplanted into 40 recipients during October 2000–July 2002. Of the remaining 47 grafts, 44 tissues were removed from distribution in July 2002, and two tissues and one organ had been discarded earlier. Of the 40 recipients, six received organs, 32 received tissues, and two received corneas. Recipients were located in 16 states and two foreign countries. All tissues had been treated with surface chemicals or antimicrobials. Bone grafts also underwent gamma irradiation.

Eight cases were identified among the 40 recipients; all cases were HCV genotype 1a. Among the six organ recipients, post-transplantation serum was available for three, and definite cases occurred in all three. Of the 32 tissue recipients, three were known to have been HCV-infected before transplantation, and test results were not available for another two (one bone and one tendon with bone recipient). Among the remaining 27 tissue recipients, five probable cases occurred: in one of two recipients of saphenous vein, in one of three recipients of tendon, and in all three recipients of tendon with bone (including the index patient). One other recipient was found to be HCV-infected after transplantation with genotype 3a. No cases occurred in recipients of skin (n = two) or irradiated bone (n = 16). Of the two cornea recipients, one was infected before transplantation. The other recipient was anti-HCV–negative; however, as of March 27, HCV RNA testing had not been performed.

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Editorial Note: This report describes transmission of HCV by tissues and organs from a donor whose serum tested anti-HCV–negative at the time of death. However, stored serum tested subsequently was HCV RNA–positive. The donor was the probable source of HCV infection for at least eight recipients of organs or tissues. All cases occurred in recipients of organs or soft tissues; no infections were found among those who had received skin or irradiated bone.

HCV transmission from tissue donors has been reported infrequently; the only tissue types reported previously to transmit HCV are nonirradiated bone and tendon with bone (*3–5*). By contrast, transplanted organs from infected donors are known to carry a high risk for transmitting HCV (*6*).

At the time of death, the donor probably was in the 8–10 week window period between infection with HCV and development of a detectable HCV-antibody response (*7*). Although available data are limited, HCV transmission by organ and tissue donors during this period appears to be uncommon; only one previous report describes HCV transmission from a tissue donor in whom anti-HCV testing (using a less sensitive first-generation assay) was negative (*3*). The frequency of transplantation from antibody-negative, HCV RNA–positive organ and tissue donors is not known. However, among voluntary blood donors, whose characteristics probably differ from those of organ and tissue donors, approximately four per 1,000,000 blood donations are from donors who are anti-HCV–negative and HCV RNA–positive (*8*).

Donor screening is the primary means of preventing transmission of viral infections from organs and tissues. The Food and Drug Administration (FDA) and the Health Resources and Services Administration (HRSA) provide regulatory guidance or oversight for screening of tissue and organ donors. In addition, organ procurement organizations are required by the Centers for Medicare & Medicaid Services to ensure that appropriate donor screening tests are performed by a laboratory certified in accordance with the Clinical Laboratory Improvement Amendments of 1988. The donor screening process includes medical chart review, interview of the donor's next of kin, physical assessment, and testing of donor serum. Guidelines require that organ and tissue donors be tested for anti-HCV.

Nucleic acid testing (NAT) to detect HCV RNA among organ and tissue donors is not performed routinely and has several limitations. Organ viability declines rapidly as a function of time after donor death. Because NAT often is not immediately accessible and can require 1–2 days to complete, it might be impractical in the setting of organ transplantation. By contrast, tissues often can be stored for months to years before use, allowing ample time for NAT. However, postmortem serum frequently is the only sample available for testing from tissue donors. NAT to detect HCV RNA has not been approved by FDA for use on serum samples obtained postmortem, and the performance of available assays in this setting has not been evaluated.

Tissue processing methods (e.g., gamma irradiation) might affect the likelihood of transmission of HCV and other viruses from infected donors (*3,9*). In this investigation, no cases occurred in recipients of irradiated bone. Irradiation is not applied routinely to all tissue types because it can impair tissue structural integrity.

This investigation was initiated by a clinician who suspected allograft-associated HCV transmission and alerted the state health department. When a new case of hepatitis C is diagnosed in a recent tissue or organ recipient, health-care providers should notify local or state health departments promptly so an investigation can be initiated and, if necessary, tissues can be recalled to prevent further transmission. Centers performing transplantation should maintain adequate records of graft recipients to facilitate investigations of allograft-associated infections.

CDC, in collaboration with FDA and HRSA, will determine whether changes in organ and tissue donor screening guidelines are warranted. Assessing the performance of available NAT and anti-HCV assays in postmortem specimens would provide essential information about the period during which donor screening can be performed reliably. Although transmission from anti-HCV–negative tissue donors probably is rare, determining the frequency of transplantations from such donors and the risk for transmitting HCV to recipients will be useful for evaluating the benefits and limitations of additional prevention measures.

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