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The Universal Data Collection Program

Report on the Universal Data Collection Program (UDC)

Special report summarizing the results from viral hepatitis testing of UDC participants

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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CENTERS FOR DISEASE CONTROL AND PREVENTION

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Single copies of the *Report on the Universal Data Collection Program* are available free from HANDI, the information service of the National Hemophilia Foundation by calling (800) 42-HANDI. Confidential information, referrals, and educational material on hemophilia and other bleeding disorders is also available through HANDI. The *Report on the Universal Data Collection Program* is accessible via internet at http://www.cdc.gov/ncidod/dastlr/Hematology/HDBarchive.htm.

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Commentary

The two most common congenital bleeding disorders are von Willebrand disease (vWD) and hemophilia. vWD is caused by defective synthesis or function of a protein, called von Willebrand factor, which is necessary for normal blood clotting. vWD occurs with equal frequency in men and women. Although the prevalence of this disease is not precisely known, it is estimated that between one and two percent of the population are affected. There are different types and severities of vWD. Symptoms include heavy or prolonged menstrual bleeding, easy bruising, frequent or prolonged nosebleeds, and prolonged bleeding following surgery, dental work, childbirth, or injury.

Hemophilia is caused by a defect in the gene located on the X chromosome that contains the genetic code for one of the clotting factor proteins necessary for normal blood clotting. A deficiency of factor VIII is referred to as hemophilia A or "classic" hemophilia. In contrast, a deficiency of factor IX characterizes hemophilia B, also known as Christmas disease. The defect usually occurs on one of the two female X chromosomes and results in a carrier state. When males have the defect on their only X chromosome, they are affected with the disease. Thus, almost all of the approximately 17,000 persons with hemophilia in the United States are male.

People with severe hemophilia can experience serious bleeding into tissues, muscles, joints, and internal organs, often without any obvious trauma. Repeated bleeding into joints without adequate treatment results in crippling chronic joint disease, one of the severe complications of bleeding disorders. In the mid-1970s, treatment for hemophilia was improved through the use of clotting factor concentrates, products made from the plasma of donated blood. However, because blood donations from thousands of donors are pooled together to make these products, many persons with bleeding disorders were infected with hepatitis B and C viruses and with human immunodeficiency virus (HIV), the virus that causes AIDS, before the risk of disease transmission in blood products was recognized and prevention measures were taken.

In 1975, Congress initiated federal funding to specialized hemophilia treatment centers (HTCs) to provide comprehensive care to persons with bleeding disorders. Since 1986, CDC has been involved with the hemophilia community through the HTC system, primarily through risk-reduction efforts aimed at preventing secondary infection of family members with HIV.

In 1991, CDC received a request from the National Hemophilia Foundation to expand their collaborative activities within the bleeding disorders community. Meetings with patients and hemophilia care providers were held during 1992 to determine the areas of highest priority. Based on recommendations from these constituents, a Congressional mandate was issued to CDC, with the goal of reducing the human suffering and financial burden of bleeding disorders by focusing national emphasis on prevention and early intervention. The issues of greatest concern identified by the bleeding disorders community were: 1) the safety of the blood supply from infectious diseases; and 2) the prevention of joint disease.

In response, CDC developed the Universal Data Collection Program (UDC). The purpose of UDC is two-fold: 1) to establish a sensitive blood safety monitoring system among persons with bleeding disorders; and 2) to collect a uniform set of clinical outcomes information that could be used to monitor the occurrence of and potential risk factors for infectious diseases and joint complications.

Persons with bleeding disorders are enrolled in UDC by care providers in each of the nation's 134 federally funded HTCs. As part of the project, a uniform set of clinical data and plasma specimens are collected by HTC staff each year during the participant's annual comprehensive clinic visit. A portion of the plasma specimen is used to perform free screening tests for hepatitis A, B, and C viruses and for HIV. The remainder of the specimen is stored for use as needed in future blood safety investigations.

Enrollment in UDC began in May 1998. Information about eligibility requirements, enrollment

procedures, and data collection can be found in the *Technical Notes* of this report. Participating HTCs are listed by region in the *Acknowledgements*. A regional map is included at the end of this report.

The purpose of this surveillance report is to disseminate the information being collected by this project to public health workers, health educators and planners, other care providers, and patients in the bleeding disorders community. The report contains information about the demographic characteristics of the participants, their blood and factor product use, and the occurrence and treatment of joint and infectious diseases. We hope that this information will prove useful to those involved in efforts to reduce or prevent the complications of these conditions.

The proper interpretation and appropriate use of surveillance data require an understanding of how the data are collected, reported, and analyzed. Therefore, readers of this report are encouraged to review the *Technical Notes*, beginning on page 14.

Suggested Reading:

CDC. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1996;45(No. RR-15):1-30.

CDC. Transmission of hepatitis C virus infection associated with home infusion therapy for hemophilia. *MMWR* 1997;46:597-599.

CDC. Occurrence of hemophilia in the United States. American Journal of Hematology 1998; 59:288-294.

Hill H, Stein S. Viral infections among patients with hemophilia in the state of Georgia. American Journal of Hematology 1998;59:36-41.

The following publications are available from HANDI (800-42-HANDI):

- *What You Should Know about Bleeding Disorders* (1997)

- *Comprehensive Care for People with Hemophilia* by Shelby Dietrich, MD (1991)

- *Understanding Hepatitis* by Leonard Seeff, MD (1997)

- *HIV Disease in People with Hemophilia: Your Questions Answered* by Glenn Pierce, MD, PhD (1991)

- *Bleeding Disorders and AIDS: The Facts* (1997)

- Information packet on von Willebrand disease.

Viral Hepatitis Testing among UDC Participants

Introduction

Transmission of viral hepatitis to persons with hemophilia has been a recognized complication of transfusion therapy with factor VIII and IX replacement products since the 1970s when these products first came into widespread use [1]. The Universal Data Collection program (UDC) was established in 1998 to serve as a national blood safety monitoring system for persons with bleeding disorders who receive treatment with these products. This special report summarizes the results from viral hepatitis testing of UDC participants for the first 2 years of the program.

Background

Beginning in the 1970s, blood banks and manufacturers of plasma-derived clotting factor replacement products introduced several measures to reduce the risk of transmission of hepatitis B virus (HBV) and what would later become known as hepatitis C virus (HCV) by these products. Blood donor testing for hepatitis B surface antigen, begun in 1971 [2-4], may have resulted in the exclusion of potential donors at high risk for HCV, thereby lowering the levels of these viruses in the plasma pools used to manufacture clotting factor. A safe and effective vaccine against HBV infection was licensed in 1981. In addition, viral inactivation steps were added during the manufacturing of clotting factor concentrates, with dry-heat inactivation licensed in the United States in 1983 and solvent-detergent inactivation in 1985. HBV screening of blood donors using the surrogate markers alanine aminotransferase (begun in late 1986) and antibody to hepatitis B core antigen (begun in early 1987) was associated with an estimated 40% decreased risk of HCV infection from blood transfusions [5]; testing for hepatitis C antibody was recommended in 1991 [6]. As a result of these measures, the risk of transfusion-related transmission of HBV and HCV was virtually eliminated by the early 1990s.

However, the viral inactivation methods that were effective against HBV and HCV were not completely effective against non-enveloped viruses, such as hepatitis A virus (HAV). Several outbreaks of HAV transmitted by clotting factor concentrates in Europe and one in the U.S. occurred in the early 1990s when solvent-detergent inactivated products predominated the market [7,8]. As a result, additional viral inactivation steps were added to decrease the risk of HAV transmission by these products.

Although currently available clotting factor concentrates (especially recombinant factor) are considered safe from contamination of viruses such as HBV and HCV, continual monitoring of blood products is necessary to ensure their safety. The UDC, a collaboration between federally funded hemophilia treatment centers (HTCs) and the Centers for Disease Control and Prevention (CDC), was initiated to monitor blood safety and the complications experienced by persons with bleeding disorders.

Upon initial enrollment in UDC, participants are tested for HAV, HBV, and HCV infection. Testing is performed according to algorithms designed to determine with the highest probability the patient's status with regard to exposure to or infection with these viruses. All participants who test negative for any of the hepatitis viruses are retested in subsequent years to monitor for seroconversions.

Prevalence of Exposure to Hepatitis Viruses

From May 1998 through June 2000, 4,736 persons with hemophilia and 889 with von Willebrand Disease (vWD) were enrolled in UDC. Laboratory testing for markers of exposure to hepatitis (i.e., antibody to HBV core antigen [anti-HBc], antibody to HAV [anti-HAV], and antibody to HCV [anti-HCV]) were performed, and data on vaccination history and risk factors for infection were collected by HTC staff to determine the prevalence of hepatitis exposure and the immune status of UDC participants.

Among persons with hemophilia, laboratory markers for exposure to HBV and HCV vary by age (Figure 1). Among persons ages 2 to 10 years at the

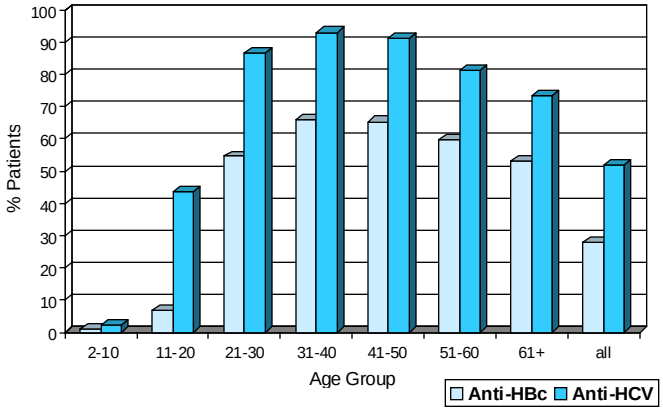


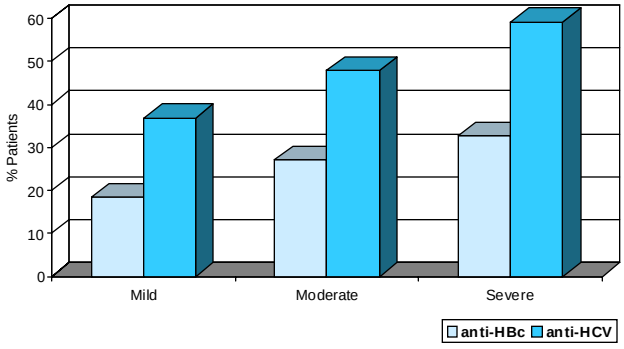
Figure 1. Prevalence of markers of infection with HBV and HCV among persons with hemophilia by age

time of UDC enrollment, the prevalence of both viruses is virtually zero. Participants in this age group were born during or after 1990 and are thus expected to be negative for exposure to these viruses because solvent-detergent treatment of replacement products was nearly universal and recombinant products were becoming widely available by the early 1990s [9, 10]. Additionally, hepatitis B immunization has been recommended for persons with hemophilia since the vaccine was first licensed in 1981 [11]. The few young hemophilic children in UDC who tested positive for these viruses were found upon further investigation to be immigrants whose initial test results in the United States were positive.

Among UDC participants with hemophilia who are older than age 21 years, 70% to 90% have been exposed to HCV. Among those 11 to 20 years old, HCV exposure drops to 40% – half that seen in the older age groups, which is similar to results reported by other investigators [12-14]. The first viral inactivation techniques, such as heat treatment, were introduced in the mid-1980s, reflecting the lower infection rates among persons currently in their mid-to-late teens.

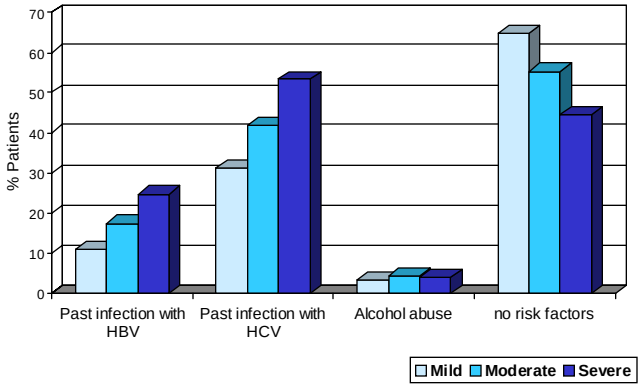
The prevalence of HBV among persons with hemophilia follows a similar distribution by age group. However, donor testing (introduced in the 1970s) and HBV vaccination (begun in the 1980s) resulted in markedly lower prevalence rates of HBV compared with HCV among individuals in the younger age groups [2-4].

The prevalence of markers for HBV and HCV is higher among persons with moderate and severe hemophilia compared to those with mild disease (Figure 2). A similar trend is apparent in data on liver disease risk factors (i.e., HBV and HCV) reported to HTC staff (Figure 3). However, the reported past infection rates for HBV and HCV are lower than the actual rates based on laboratory testing, indicating under-reporting of these infections by HTC staff on the annual visit forms. As expected, alcohol abuse, a risk factor for liver disease not related to replacement product exposure, has a low prevalence that does not vary by hemophilia severity.



Mild, N=900; Moderate, N=974; Severe, N=2370

Figure 2. Prevalence of markers of infection with HBV and HCV by hemophilia severity



Mild, N=1078; Moderate, N=1142; Severe, N=2777

Figure 3. Reported risk factors for liver disease by hemophilia severity

The prevalence of markers for HBV and HCV is uniformly lower among persons with vWD than among those with hemophilia (Figure 4). The relatively high prevalence of HCV in the 21-30

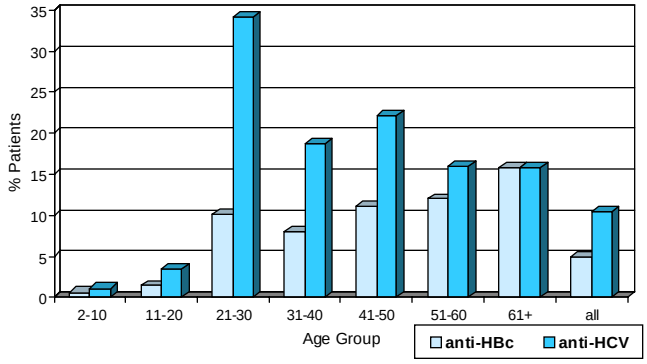
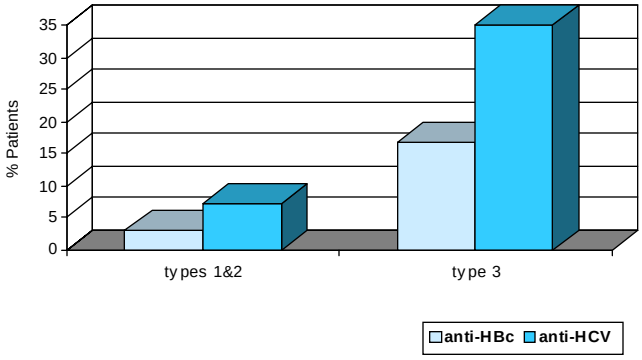


Figure 4. Prevalence of infection with HBV and HCV among persons with vWD by age

year-old age group is due to the high proportion of patients in this age group who have type 3 vWD, the most severe form of the disease. Persons with type 3 vWD have bleeding tendencies similar to those of persons with hemophilia and are more likely to receive blood products than persons with with types 1 and 2 vWD. As a result, the type 3 patients have a much higher prevalence of markers for HBV and HCV compared with persons with types 1 and 2 vWD (Figure 5).



Types 1 & 2, N=610; Type 3, N=83

Figure 5. Prevalence of markers of infection with HBV and HCV by vWD type

HBV and HAV Vaccination among UDC Participants

CDC has recommended universal hepatitis B vaccination of infants since 1991 [15] and vaccination of high-risk individuals, including persons with hemophilia, since the vaccine was first licensed in 1981 [11]. More than 90% of persons ≤20 years of age enrolled in UDC have been vaccinated against HBV infection (Figure 6). Most older hemophilic UDC participants developed their immunity naturally due to infection with HBV prior to the development of the vaccine.

In general, the proportion of persons who have immunity to HBV is lower for those with vWD compared with persons with hemophilia (Figure 7). In contrast to persons with hemophilia, however, most UDC participants with vWD who have antibodies to HBV obtained their immunity through vaccination. The Medical and Scientific Advisory Council to the National Hemophilia Foundation has recommended that any individual with a congenital bleeding disorder who was not vaccinated at birth should be vaccinated against HBV at the time of diagnosis [16].

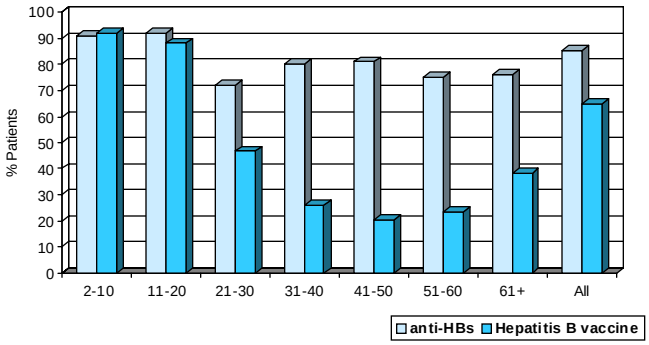


Figure 6. Prevalence of natural or acquired immunity to HBV and reported vaccination among persons with hemophilia

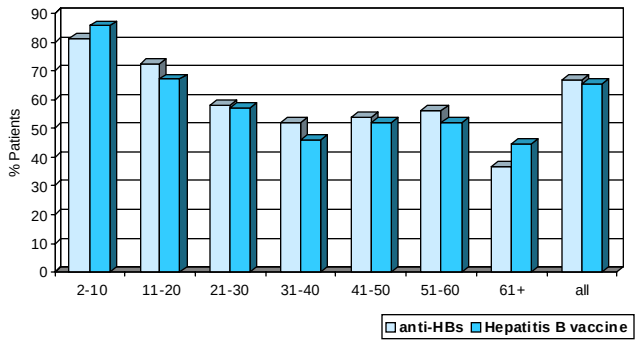


Figure 7. Prevalence of natural or acquired immunity to HBV and reported vaccination among persons with vWD

Recommendations to vaccinate persons with bleeding disorders against HAV infection were made as soon as the vaccine was licensed in 1995 [17]. Prior to that time, several outbreaks of HAV infection had occurred among users of solvent-

detergent treated, plasma-derived products [7, 8], Vaccination rates for HAV are lower than those for HBV among both persons with hemophilia (Figure 8) and those with vWD (Figure 9). The high prevalence of antibodies to HAV among the older age groups in the absence of vaccination implies exposure to HAV, either through blood products manufactured prior to the institution of viral inactivation steps or community-acquired infection. Among individuals older than 30 years of age, anti-HAV prevalence is much higher among those with hemophilia compared to those with vWD, the latter of which have a prevalence similar to that seen in the general population (as above).

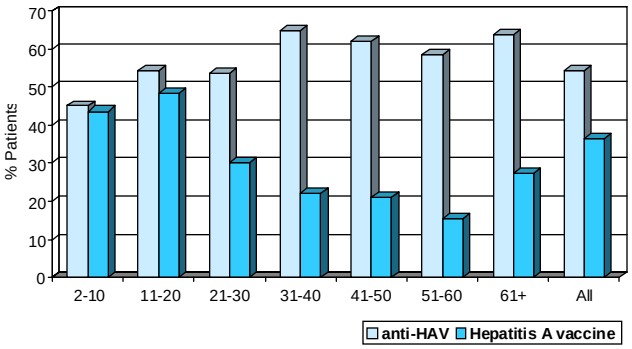


Figure 8. Prevalence of natural or acquired immunity to HAV and reported vaccination among persons with hemophilia

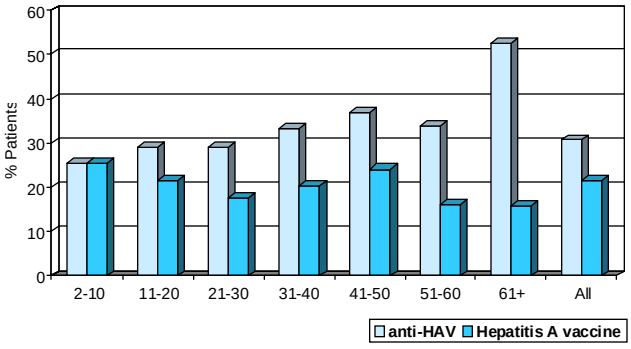


Figure 9. Prevalence of natural or acquired immunity to HAV and reported vaccination among persons with vWD

Hepatitis A vaccination is particularly important for persons who are infected with HCV. For example, persons with HCV-related chronic liver disease are at increased risk of death from liver failure as a result of acute HAV infection [18]. Among HCV-infected UDC participants, a greater proportion have either natural or acquired immunity to HBV than to HAV (Figure 10). Immunity rates range from 61% to 65% for HAV and from 75% to 83% for HBV, with higher rates occurring among persons with hemophilia compared with those with vWD. Additionally, among persons with hemophilia, immunity rates vary by disease severity from 53% (mild) to 68% (severe) for HAV and from 77% to 84% (mild to severe, respectively) for HBV (Figure 11).

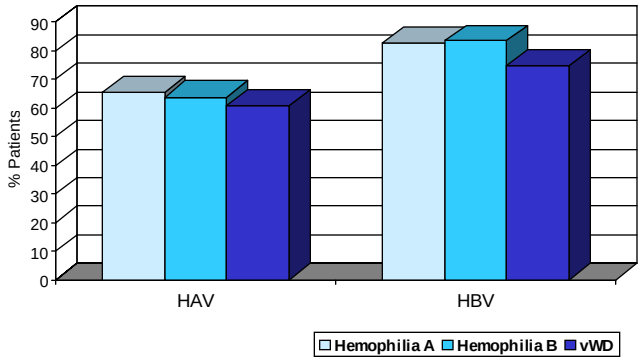


Figure 10. Natural and acquired immunity to HAV and HBV among HCV-infected persons

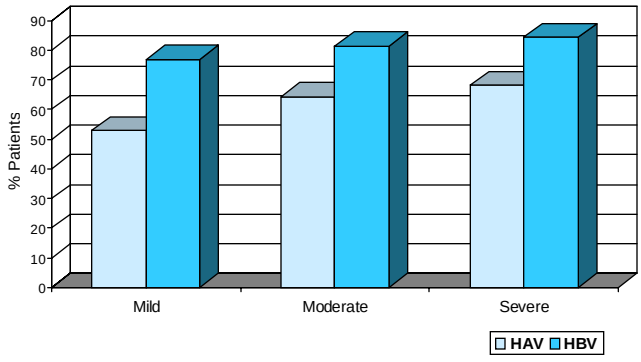


Figure 11. Natural and acquired immunity to HAV and HBV by severity of hemophilia among persons with hemophilia infected with HCV

Monitoring Blood Safety

From May 1998 through June 2000, 1,358 participants participated in UDC for more than one year. Possible seroconversions were identified for a) HAV based on total anti-HAV test results, and acute infection was identified by IgM anti-HAV; b) HBV based on any marker for acute or chronic infection or immunity to infection and included anti-HBs, total anti-HBc, HBsAg, and HBeAg; and c) HCV based on anti-HCV test results. Persons whose test results changed from negative in the first year to positive in a subsequent year were investigated

in a step-wise manner. First, laboratory results were compared with information about past infections and vaccinations provided by HTC staff on annual visit and laboratory forms. If the change in laboratory results could not be explained on the basis of information obtained from these forms, CDC staff contacted the treatment center staff for clarification of existing data and for additional information. In some cases, resolution of the discrepancy could only be accomplished by repeat testing – most often performed on the previously drawn specimens. Less frequently, repeat testing was performed on newly drawn specimens.

Investigation Results

Hepatitis A Virus

Among the 1,358 UDC participants, 239 persons (18%) were identified who appeared to seroconvert from HAV negative in year 1 to HAV positive in year 2 (Table 1). Based on information obtained either from the annual visit or laboratory data forms or from discussions with HTC staff, 172 of these persons (72%) had received either the full or partial vaccination series in the interval between testing. Twelve persons (5%) had low positive results in the second year that most likely represented false-positive tests. After retesting available specimens, 46 persons (19%) were found to have had false negative anti-HAV results in year 1. Investigation of the remaining 9 individuals revealed the following potential explanations for their apparent seroconversion: 6 persons were HIV-infected (HAV antibodies may have gone undetected in year 1); 1 person had a positive anti-HAV result in the distant past (probable false-negative test in year 1); 1 participant appeared to be anti-HAV positive in year 2 due to passive transfer of anti-HAV from transfusion with fresh frozen plasma; and 1 individual was thought by treatment center staff to have been exposed to HAV during recent travel in Mexico. None of the participants identified with possible seroconversions had a positive test for IgM anti-HAV that was indicative of acute infection with HAV.

Table 1. Investigation results for 239 apparent HAV seroconversions among UDC participants, 1998-2000

HAV Marker	Investigation Result	Number
Anti-HAV	False-negative test in year 1	46
	False-positive test in year 2	12
	Vaccination between year 1 and year 2	172
	Other*	9

*Please see text for details.

Hepatitis B Virus

Among the 1,358 UDC participants, 50 persons (4%) were identified who appeared to seroconvert from HBV marker negative in year 1 to HBV marker positive in year 2 (Table 2). Of these, 34 (68%) had a change in anti-HBs status, 15 (30%) had a change in anti-HBc status, and 1 (2%) had a change in HBeAg status.

Of the 34 persons with a positive anti-HBs in year 2, 19 (56%) had received either vaccination or booster in the interval between testing based on information obtained either from the annual visit or laboratory data forms or from discussions with HTC staff. One person with no previous history of infection had low positive results in the second year that most likely represented a false-positive test result. After retesting available specimens, the remaining 14 persons (41%) were found to be negative for anti-HBs in year 1. Of these, 3 participants had low titers (≤10/mlU/ml) of anti-HBs, despite annual visit form information indicating previous vaccination. Although a booster was recommended by the UDC testing laboratory, it is unknown whether these patients received additional vaccine. Vaccine-induced antibodies decline gradually with time, and as many as 60% of those who initially respond to vaccination will lose detectable anti-HBs by 8 years [19]. While an individual clinician may choose to give additional doses of vaccine, booster doses of vaccine are not routinely recommended because persons who respond to the initial vaccine series remain protected against clinical hepatitis and chronic infection, even when their anti-HBs levels become low or undetectable [15,20].

Among the 15 persons with anti-HBc changes, 10 (67%) had a history (by patient report and serologic evidence) of past infection with HBV and, therefore, had false-negative year 1 results. Of these, 6 were HIV positive, which may have contributed to the false-negative tests. The other 5 participants with anti-HBc changes did not have a history of previous infection. One person was found to have had a false-positive anti-HBc in year 2 when the specimen was re-tested. The remaining 4 participants had low anti-HBc ratios (≤1.2) in year 2, which most likely represented false-positive results.

The person whose HBeAg shifted from negative in year 1 to positive in year 2 was known to have a long-standing chronic HBV infection. Therefore, fluctuating levels of antigen associated with changes in disease activity were most likely responsible for the negative HBeAg result in year 1.

Table 2. Investigation results for 50 apparent HBV seroconversions among UDC participants, 1998-2000

HBV Marker	Investigation Result	Number
Anti-HBs	Negative test in year 1	14
	False-positive test in year 2	1
	Vaccination/booster between years 1 and 2	19
Anti-HBc	False-negative test in year 1	10
	False-positive test in year 2	5
HBeAg	Negative test in year 1,secondary to fluctuating HBeAg	1

Hepatitis C Virus

Among the 1,358 UDC participants, 4 persons (0.3%) were identified who appeared to seroconvert from HCV negative in year 1 to HCV positive in year 2 (Table 3). For one participant with a known history of HCV infection prior to enrollment, confirmatory RIBA and PCR testing for HCV RNA documented the false-negative anti-HCV result in year 1. Infection with HIV was a possible contributing factor in this case. The remaining 3 participants had false-positive results in year 2 on the basis of negative or indeterminate RIBA tests and negative PCR for HCV RNA on the specimens from year 2. None of these persons had a known history of HCV infection prior to UDC enrollment. Additionally, all were under 11 years of age and thus would not have been at increased risk for exposure to HCV-contaminated blood products.

Table 3. Investigation results for 4 apparent HCV seroconversions among UDC participants, 1998-2000

HCV Marker	Investigation Result	Number
Anti-HCV	False-negative test in year 1	1
	False-positive test in year 2	3

Conclusions

UDC was established to monitor the safety of blood and blood products used by persons with bleeding disorders. Based on our review of test results from 1,358 persons with bleeding disorders, several positive conclusions may be drawn. First, no new infections with HAV, HBV, HCV, or HIV were identified among UDC participants during the first 2 years of the surveillance. Second, the public health message to vaccinate this high-risk population is being implemented. Of the changes found in anti-HAV status among participants, 72% were attributed to hepatitis A vaccinations administered between years 1 and 2. Among persons who had a change in anti-HBs from years 1 to 2, 56% had received primary hepatitis B vaccination or booster administrations resulting in these changes.

The Advisory Committee on Immunization Practices (ACIP) has issued several guidelines for vaccinating persons against hepatitis A and B virus infections. For HBV, universal vaccination is recommended for all infants [15]. UDC data as of March 2000 indicate that approximately 92% of hemophilic children younger than 4 years of age had been vaccinated against HBV. This compares favorably with 87% of all children between the ages of 18-35 months receiving the three-dose hepatitis B

vaccine series [21]. In 1996, ACIP recommended that persons at increased risk for contracting HAV infection be vaccinated [17]. Persons with hemophilia were specifically mentioned as being at high risk for developing HAV infections through their use of replacement products. Furthermore, persons with bleeding disorders who are chronically infected with HCV are at risk of serious complications from HAV infection – an additional incentive for vaccination.

The nation's blood supply is safer now than at any time in the past. However, monitoring is important to ensure the continued safety and to detect the emergence of new pathogens that may pose a potential threat to the blood supply. The UDC plays an important role in this surveillance by closely monitoring a unique population that has a high level of exposure to blood products.

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21. Centers for Disease Control and Prevention. Immunization of infants 18-35 months old. MMWR 1999;48(37);829-830.
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Eligibility Requirements

To participate in UDC, patients must receive care in a federally funded HTC and meet at least one of the following criteria: 1) age 2 years or older with a bleeding disorder due to congenital deficiency or acquired inhibitors in which any of the coagulation proteins is missing, reduced, or defective and has a functional level of less than 50 percent; or 2) age 2 years or older with a diagnosis by a physician of vWD. Individuals specifically excluded from participation in UDC include persons with any of the following: 1) an exclusive diagnosis of a platelet disorder; 2) thrombophilia; or 3) coagulation protein deficiencies due to liver failure.

Data collection

UDC data are collected during the participant's "annual visit," which ideally should occur once each calendar year (January-December), with the interval between visits as close as possible to 12 months. Data are collected according to guidelines and definitions detailed in surveillance manuals provided to HTC staff by CDC. Informed consent for participation is obtained each year. Demographic information and reasons for refusal are obtained using a Patient Refusal Form for all eligible persons who decline participation. To protect patient confidentiality, all data sent to CDC do not contain personally identifying information, but rather use a unique 12-digit code that is generated by a computer software program supplied to HTCs by CDC.

Eligible participants are registered into UDC through a Registration Form completed by HTC staff; this form includes patient demographic, diagnostic, and historical information. Month and year of birth are used to calculate age on the last day of the current year. Information on race and ethnicity is obtained from clinic records and may have been based either on self-report or on observations made by care providers.

During the annual visit, clinical information is recorded on a standardized data collection form (Annual Visit Form). In addition to information about education, employment status, and health insurance, data are also collected about treatment type (episodic vs. prophylactic), presence and treatment of inhibitors, the number of bleeding episodes experienced (based on infusion logs or patient recall), type and brand name of all factor concentrates or other treatment products used, and whether or not clotting factor is infused at home.

Information regarding infectious diseases is also collected including risk factors and clinical signs, symptoms, and laboratory markers of liver disease. Data are also recorded about any therapy for chronic hepatitis, the status of vaccination for hepatitis A and B viruses, and, among patients with an intravenous access device, the occurrence of a device-associated infection. Persons $\geq$16 years of age who are HIV-infected are asked several questions concerning risk-reduction activities including partner testing and condom use.

Data are also collected on joint disease, including the use of walking aids, the occurrence of joint infections, and measures of impact of joint disease on daily activities. During the visit, range of motion measurements on five joints (hip, knee, shoulder, elbow, and ankle) are taken by a physical therapist or other trained health care provider according to detailed guidelines provided in a reference manual supplied by CDC. All health care providers performing these measurements are trained and certified by regional physical therapists who have themselves received centralized training. In addition, information about whether a particular joint is a "target joint" or whether the participant has required the use of an orthopedic appliance or has undergone an invasive orthopedic procedure is collected. In UDC, a target joint is defined as a joint in which recurrent bleeding has occurred on four or more occasions during the previous 6 months.

All data collection forms are sent overnight to CDC where they are then key entered into a computer database using double-entry software to minimize data-entry errors. Data are then screened for omissions, inconsistencies, and unusual values that possibly represent abstraction or data-entry errors.

Error reports are generated and faxed to the HTC, where a designated UDC contact uses available information to resolve discrepancies and complete missing data items.

Laboratory testing

During the annual visit, a blood specimen is obtained from each participant in UDC. The specimen is processed by HTC personnel according to guidelines provided by CDC that are designed to minimize the effects of storage and shipment on subsequent analyses. Samples are shipped overnight to the CDC Serum Bank where they are aliquoted and stored. A portion of the specimen is sent to the Eugene B. Casey Hepatitis Laboratory at Baylor College of Medicine in Houston, Texas. A second portion is sent to the HIV Testing Laboratory at CDC. The remainder of the specimen is stored in the CDC Serum Bank for future blood safety investigations, as needed.

Testing for hepatitis A, B, and C viruses follow algorithms designed to determine with the highest probability the patient's status with regard to exposure to or infection with these viruses. Information provided by HTC staff on a Laboratory Form, including the results of previous local testing and vaccination history, is used by personnel at the testing laboratory to provide a detailed interpretation of the test results.

Testing for HIV follows algorithms designed to determine patient status with regard to infection with HIV-1 and HIV-2. The results of all laboratory testing are reported to the HTC using the CDC unique code which can be matched to the patient only by HTC staff.

Mortality reporting

Deaths occurring among all HTC patients (regardless of whether or not they have been enrolled in UDC) are reported to CDC using a Mortality Form. Data collected include age at death, sex, race/ethnicity, disease type and severity, and whether or not blood products had been used during the year prior to death. Additionally, information about the death, including the date, cause (primary and contributing), and whether or not an autopsy was performed, is also collected.

Tabulation and presentation of data

Data in this report are provisional. The data presented in this report represent the first 22 months of what is planned to be at least a 5-year surveillance project. Future reports will include expanded data tables to cover subsequent surveillance periods and will provide the results of more detailed analyses of available data and findings from special studies.

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New England Hemophilia Center
Worcester, MA
Dartmouth-Hitchcock Hemophilia Center
Lebanon, NH
Rhode Island Hospital
Providence, RI
UCONN Hemophilia Treatment Center
Farmington, CT
Vermont Regional Hemophilia Center
Burlington, VT
Boston Children's Hospital
Boston, MA
Yale University School of Medicine
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Puerto Rico Hemophilia Treatment Center
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Newark Beth Israel Medical Center
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UHSH Blood Disorders Center
Johnson City, NY
The Mount Sinai – NYU Medical Center / Health
System, New York, NY
Long Island Jewish Medical Center
New Hyde Park, NY
The New York Presbyterian Hospital
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Region III *Sue Cutter, M.S.W., M.P.A.*
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Georgetown University Medical Center
Washington, DC
University of Virginia Hospital
Charlottesville, VA
Virginia Commonwealth University
Richmond, VA
Children's Hospital of the King's Daughters
Norfolk, VA
Cardeza Foundation Hemophilia Center
Philadelphia, PA
Christiana Care Health Services
Newark, DE
Hemophilia Center of Central Pennsylvania
Hershey, PA
Hemophilia Center of Western Pennsylvania
Pittsburgh, PA
West Virginia University Medical Center
Morgantown, WV
Charleston Area Medical Center
Charleston, WV
Johns Hopkins University Medical Center
Baltimore, MD
Children's Hospital of Philadelphia Speciality
Center, Voorhees, NJ
Children's Hospital of Philadelphia
Philadelphia, PA
Lehigh Valley Hospital
Allentown, PA

St. Agnes Hospital
Baltimore, MD
Penn Comprehensive Hemophilia Program
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Region IV-N
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Brown Cancer Center
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Children's Hospital of Palmetto-Richland
Memorial, Columbia, SC
University of Tennessee – Memphis
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Vanderbilt University Medical Center
Nashville, TN
University of North Carolina at Chapel Hill
Chapel Hill, NC
Norton Kosair Children's Medical Center
Louisville, KY
East Carolina University
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East Lansing, MI
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Eastern Michigan Hemophilia Treatment Center
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Minneapolis, MN
Mayo Clinic
Rochester, MN
MeritCare Hospital DBA Roger Maris Cancer
Center, Fargo, ND
Hemophilia Outreach Centre
Green Bay, WI
Gunderson Clinic
LaCrosse, WI
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Madison, WI
Rush Children's Hospital
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Michael Reese Hospital – Adult
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South Texas Comprehensive Hemophilia Center
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Los Angeles, CA
Children's Hospital, San Diego
San Diego, CA
Children's Hospital of Orange County
Orange, CA
Children's Hospital Oakland
Oakland, CA
Hemophilia and Thrombosis Center of Nevada
Las Vegas, NV
Guam Comprehensive Hemophilia Care Program
Agana, GU
City of Hope National Medical Center
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Valley Children's Hospital
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