

Transmission of Hepatitis C Virus Through Transplanted Organs and Tissue — Kentucky and Massachusetts, 2011

On September 29, 2011, the United Network for Organ Sharing notified CDC of two patients who tested positive for hepatitis C virus (HCV) infection approximately 6 months after receiving kidney transplants from a deceased donor. Before transplantation, the donor had tested negative for HCV antibody by the organ procurement organization. Tissue also was procured from the donor for possible transplantation. The tissue bank performed an HCV antibody test on the donor's serum specimen that was negative and nucleic acid testing (NAT) that was positive, but misread as negative. Retesting of the donor specimen during the investigation confirmed the NAT results as positive. Donated tissue included 43 musculoskeletal grafts and one cardiopulmonary patch, which were distributed to health-care facilities in several states. An investigation was initiated to 1) identify potential sources of the donor's infection, 2) document the mode of transmission to the organ recipients, and 3) ensure timely notification of the implanting surgeons and testing of tissue recipients. Implantation of infected HCV tissue occurred after recognition of new HCV infection in the organ transplant recipients, highlighting the need for rapid communication between transplant centers, organ procurement organizations, tissue banks, and public health authorities regarding suspected transplantation transmission events.

Donor Investigation

The donor, a middle-aged man in Kentucky, sustained a traumatic brain injury in March 2011 in an all-terrain vehicular incident and died 2 days later. His medical history was significant for schizophrenia, substance abuse, and a 5-month incarceration approximately 10 years before his death. The donor had no known history of intravenous drug use or other hepatitis risk factors, according to his father at the time of organ procurement; however, further investigation revealed that the donor's father had limited contact with his son during the year before his death and was unfamiliar with recent personal habits or behaviors.

Policies of the Organ Procurement and Transplantation Network (OPTN), the oversight entity for solid organs in the United States, require testing for HCV by antibody only, whereas the Food and Drug Administration (FDA), which regulates human cells, tissues, and cellular and tissue-based products, requires screening of donated tissue for HCV by both antibody and NAT (1). The donor's HCV antibody tested negative on both organ and tissue donor screening, but misreading of the reaction wells on testing led to an incorrectly reported negative HCV NAT result. Once this error was identified, repeat NAT was performed at the tissue bank and confirmed that the donor was HCV-positive at the time of donation. During the donor's final hospital stay in March, he received six units of blood products. Pretransfusion serum from the donor was not available for analysis. Testing of posttransfusion stored serum at CDC on October 28 confirmed by NAT that the donor was HCV-positive with genotype 1a and a viral load of >69,000,000 IU/mL. Blood traceback investigation of the six associated blood donors to the infected donor is ongoing, and all remaining units from these donations have been quarantined.

Organ Transplant Investigation

In March 2011, three organs (two kidneys and the liver) from the donor were transplanted into three recipients at a local hospital in Kentucky (Figure). Both kidney recipients had

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tested negative for hepatitis C before transplant, whereas the liver recipient had a previous diagnosis of hepatitis C.

First kidney recipient. On July 26, 2011, the recipient of the first kidney, a man aged 41 years, was noted to have elevated liver enzymes (aspartate aminotransferase [AST]: 161 U/L; alanine aminotransferase [ALT]: 217 U/L). HCV antibody testing conducted August 22 was negative. Liver function tests continued to be elevated, and HCV NAT performed September 19 was positive.

Second kidney recipient. The recipient of the second kidney, a woman aged 46 years, was noted to have elevated liver function tests on August 25 (AST: 206 U/L, ALT: 221 U/L); HCV NAT was positive September 21.

Liver recipient. The liver recipient, a man aged 51 years, had a history of chronic infection with HCV, genotype 1a, before transplant. Liver function testing on September 7 was unchanged from his baseline (AST: 46 U/L, ALT: 55 U/L).

At CDC, serum specimens were tested for HCV RNA. Serum collected after organ transplantation from all three recipients tested positive for HCV by NAT at CDC, and all three HCV strains were confirmed to be genotype 1a.

Tissue Transplant Investigation

On September 29, the organ procurement organization notified the tissue bank of the apparent HCV transmission to the kidney and liver recipients. The tissue bank informed health-care facilities, and a voluntary recall was begun on

September 30. The tissue bank had distributed 43 musculoskeletal grafts and one cardiopulmonary patch to health-care facilities, but names and contact information for surgeons who implanted these tissues were not uniformly available at the time of recall. CDC telephone notification of all surgeons and requests for testing of all patients was completed on October 27.

The cardiopulmonary patch, the only nonmusculoskeletal tissue distributed, had been treated with antibiotics by the tissue bank according to protocol and was implanted by a health-care facility in Massachusetts on September 26. After the health-care facility was notified, the recipient underwent testing. Hepatitis C antibody was negative, but NAT was positive at 82,000 IU/mL; the recipient's ALT was normal (12 U/L).

The 43 distributed musculoskeletal grafts were treated chemically and by irradiation at the tissue bank, according to protocol. Fifteen of the musculoskeletal tissues were implanted; the remaining 28 were returned to the tissue bank. The 15 recipients of musculoskeletal tissues were recommended to receive HCV serologic testing and NAT immediately and again 6 months from the time of tissue implantation. As of December 16, initial test results from 14 of the musculoskeletal tissue recipients were known, and all were negative based on HCV NAT.

Molecular Characterization of HCV Strains

To determine the genetic relatedness among the HCV strains obtained from the donor, the two kidney recipients, the liver

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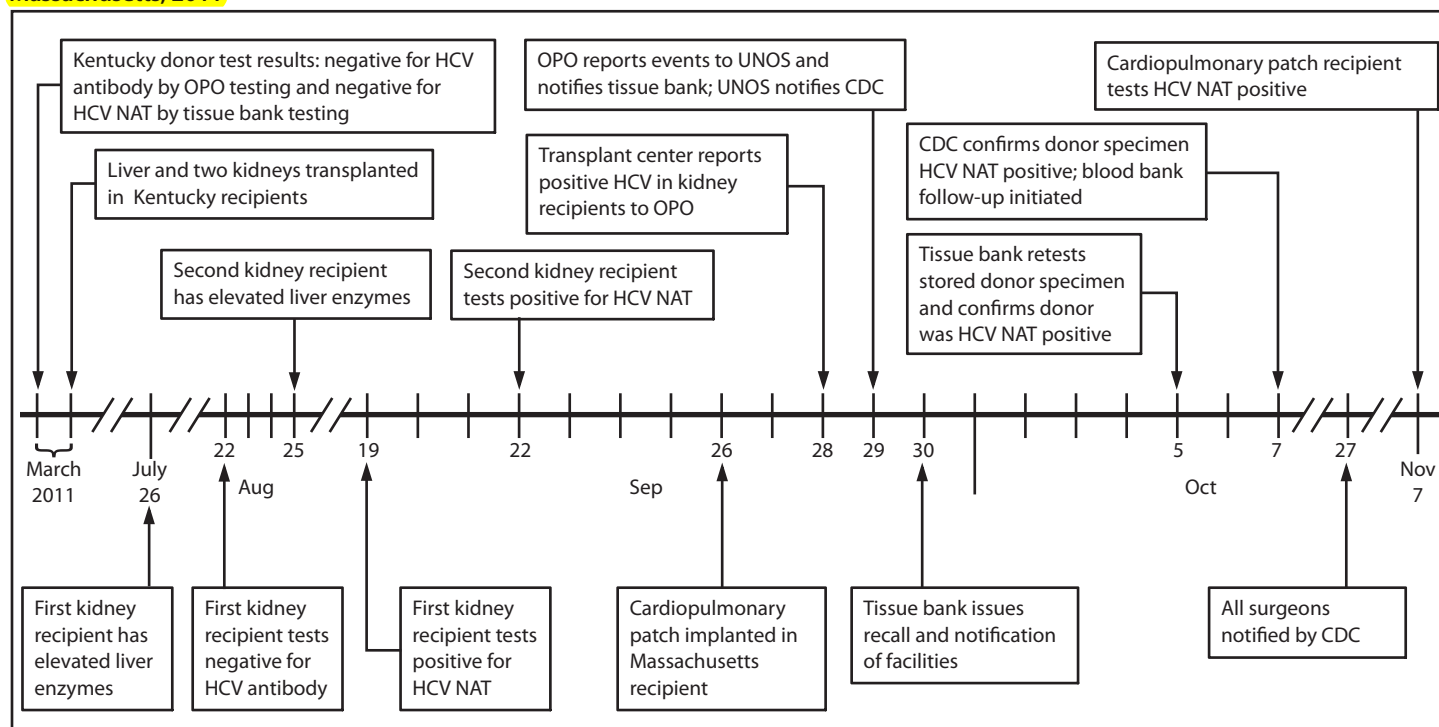
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FIGURE. Investigation timeline after initial report of transmission of hepatitis C virus (HCV) from an organ and tissue donor — Kentucky and Massachusetts, 2011

Abbreviations: OPO = organ procurement organization; NAT = nucleic acid testing; UNOS = United Network for Organ Sharing.

recipient, and the cardiopulmonary patch recipient, maximum likelihood phylogenetic trees were created (2). These analyses showed that two specimens from the donor and the three specimens from the kidney recipients and cardiopulmonary patch recipient shared identical NS5b sequences; the liver recipient did not share these sequences, indicating previous infection. Quasispecies analysis was performed on the specimens that shared identical NS5b sequences (3). The E1-HVR1 quasispecies sequences from the donor, the two kidney recipients, and the cardiopulmonary patch recipient clustered in a single group, indicating their close genetic relatedness consistent with a common source of HCV transmission. The donor and the two kidney recipients and one cardiopulmonary patch recipient had from two to 10 distinct E1-HVR1 sequences that shared from 99.7% to 100% similarity with each other.

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Editorial Note

The transmission of HCV associated with transplanted organs and minimally processed tissue has been described previously, but this is the first recognized HCV transmission via a cardiopulmonary patch (4). Although correct reading of tissue donor NAT screening results would have prevented transmission through the tissue patch, the organ recipients still would have become infected because current OPTN policies for organ donor screening only require HCV serologic testing (1). Furthermore, positive organ donor NAT screening likely would have resulted in quarantine of potentially infected tissue. Use of NAT, in addition to anti-HCV serologic testing, has been proposed to decrease the risk for transmitting undetected HCV infection. However, no one test can uniformly detect all infections, either because of false-negative tests resulting from the window period, or assay-related issues, or, as described in this report, because of human error.

What is already known on this topic?

Hepatitis C virus (HCV) transmission from antibody-negative organ donors has been documented previously; nucleic acid testing (NAT) is required for tissue donors but not for organ donors.

What is added by this report?

A donor transmitted HCV to two kidney recipients and one tissue recipient because of a negative antibody test (a result of the window period) and an incorrectly read HCV NAT result. Implantation of infected tissue occurred after recognition of the infected organ transplant recipients, highlighting the need for more rapid methods to recognize and communicate information on suspected transplantation transmission.

What are the implications for public health practice?

HCV antibody testing alone might not be adequate to detect disease in organ donors with acute infection or in recipients who are immunosuppressed. A real-time system for notification of disease clusters in transplant recipients is needed to prevent further use of tissue that tests positive for HCV or other infections. Suspected disease transmission through organ and tissue transplantation should be reported by clinicians to appropriate oversight organizations and public health authorities without delay.

Without information regarding a donor's behavioral risk factors, the assay selection and sensitivity of pretransplantation testing is critical. The incidence of HCV infection not detected by serologic screening for anti-HCV antibody varies from 1 in 5,000 for normal-risk patients to 1 in 1,000 for patients at high risk (5). The window period (i.e., the time from exposure to detectable HCV antibody) has a mean of 65–70 days; this period is shortened to 3–5 days with use of NAT (6). A transplant facility's decision to use an organ is based on the organ procurement organization's assessment of the donor's risk status and on test results (5). Multiple factors, including the urgent need for a potentially life-saving transplant and informed consent of the transplant candidate must be considered when determining whether benefits of transplantation outweigh the risk for transmitting HCV. The U.S. Public Health Service recently drafted guidelines recommending testing of all organ donors with NAT for HCV regardless of risk status (7). Even if test results are not available at the time of transplantation, results still can be used afterward to guide recipient evaluation and treatment.

The diagnosis of HCV infection in two recipients of kidneys from the same donor should raise immediate suspicion of donor-derived infection and reporting to OPTN and to local and state health departments as required by policy. Reporting to local and state health departments also should occur because acute HCV infection is a nationally notifiable disease. Reporting of suspected new diagnoses in organ recipients, including to tissue banks, should occur without delay, because such diagnoses might have implications for tissues that have not yet been transplanted.

The events in this report demonstrate the importance of timely communication once a transplant transmission is suspected and the difficulty of tracking tissue to the patient or provider level should a potential transmission be recognized after tissue has been distributed. Although FDA requires that the tissue bank track the distribution of tissues down to the institutional level, no government regulations require tracking tissue to the patient level; hospitals are asked voluntarily to return a record, often a postcard, to the tissue bank to notify them of implantation of the tissue. Many health-care facilities have a mechanism to track tissue to the patient, although approaches are not standardized (8). Systems that facilitate real-time notification of possible disease transmission to tissue banks, organ procurement organizations, and other transplant centers do not exist, and development is hindered by the lack of standardized tissue nomenclature and identification standards (9,10).

This investigation reveals several areas in which current detection and notification might be improved to prevent similar future transplant transmission events, including: 1) consideration of the use of HCV NAT for organ donors; 2) use of algorithms or other procedures to ensure accurate reading of test results and reduce human error; and 3) timely feedback of possible disease transmission in organ or tissue recipients to organ procurement organizations, tissue banks, public health authorities, and regulators.

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Food Safety Epidemiology Capacity in State Health Departments — United States, 2010

In 2002, the Council of State and Territorial Epidemiologists (CSTE) conducted its first national food safety epidemiology capacity assessment (1), which provided the basis for development of minimum performance standards to guide state and local foodborne disease control programs. During April 2010, CSTE sent states a follow-up, web-based questionnaire to gather information about food safety–related workforce training and education, epidemiology and laboratory capacity, and information technology (IT) to support surveillance. This report summarizes the results of the assessment, which found that in 2010, states reported a need for 304 more full-time equivalent (FTE) employees working in food safety to reach full program capacity, with the greatest demand for master's degree–level epidemiologists (50% of demand). Barriers to investigating foodborne outbreaks reported most often by states included delayed notification of the outbreak (reported by 41 states), lack of a sufficient number of foodborne safety staff members (29 states), lower prioritization of investigations (27 states), lack of ability to pay overtime (20 states), and lack of adequate epidemiology expertise (12 states). Strategies should be developed to increase the number of food safety staff members and enhance their training opportunities, address gaps in IT, and improve the relationship between state and local health departments and federal agencies collaborating on responses to foodborne disease outbreaks.

The main objectives of the food safety epidemiology capacity assessment were to count and characterize the food safety workforce in local, regional, and state health departments and to measure and evaluate core capacity to detect, investigate, and respond to foodborne diseases and outbreaks. After pilot testing, CSTE made the assessment available online to all states during April 2010. The assessment was sent to the state epidemiologist and the lead foodborne disease epidemiologist in each state, with a suggestion for the latter to serve as respondent. All 50 states participated, but not every state answered all questions. Capacity was defined for participants using a qualitative scale,* as validated in previous CSTE assessments (2–4).

In 2010, a total of 787 FTEs were working as foodborne disease epidemiologists in state, regional, and local health departments in the United States. Of these, 616.5 (78%) had an epidemiology-related degree or had completed some coursework in epidemiology; 170.5 (22%) had only on-the-job

training or no formal epidemiology training (Table). Formal education in epidemiology was highest at the state level, where most (73%) foodborne disease epidemiologists had an epidemiology degree. The proportion of personnel working as foodborne epidemiologists who had a nursing degree was substantially higher at the local level (19%) than at the regional (5%) or state (4%) level. States reported the need for an additional 304 FTEs to reach full program capacity, with the greatest demand (50% of need) for master's-level epidemiologists.

The number of respondents with substantial-to-full capacity to use electronic laboratory reporting for foodborne diseases by laboratory type was highest for public health laboratories and lower for other laboratory types (i.e., hospital-based, reference, and other clinical). Forty-three states reported using a National Electronic Diseases Surveillance System–compliant database for maintaining enteric illness cases. Forty-two states reported using an electronic database housed at the state health department for outbreak investigations; 13 states used an electronic database at the local level. All respondents used CDC's electronic Foodborne Outbreak Reporting System and National Outbreak Reporting System for reporting. Most states electronically recorded multiple variables related to cases of enteric illness, including laboratory results (49 states), epidemiologic risk factors (44), clinical symptoms (42), travel history (42), environmental exposures (42), food history (35), and food purchasing locales (30), as separate elements of their enteric illness case files.

State capacity for completing tasks related to the investigation of sporadic cases of enteric illness caused by *Salmonella* and *Escherichia coli* O157 varied. Nearly all (49) states entered case data electronically for both pathogens; other tasks were generally more likely to be completed for *E. coli* O157 than for *Salmonella*, including collection of isolates (48 and 46 states, respectively), pulsed-field gel electrophoresis analysis (48 and 42), analysis of aggregate data (46 and 45), comparison of case classification to standard case definition (49 and 44), interview of patients (47 and 39), and more intensive questionnaire review (42 and 38).

Although states investigate foodborne disease outbreaks caused by numerous pathogens, they were more likely to investigate outbreaks associated with some pathogens than others. For specific pathogens, a history of investigating >75% of outbreaks was reported by the highest proportion of states for *E. coli* (86% of states), followed by *Listeria* (81%), *Salmonella* (78%), *Campylobacter* (73%), other foodborne pathogens (68%), and norovirus (55%). Conversely, a small but substantial proportion of states reported investigating <25% of outbreaks caused by these same pathogens: *Campylobacter*

*None means that none of the activity, knowledge, or resources described within the question were met; minimal capacity = 1%–24%, partial capacity = 25%–49%, substantial capacity = 50%–74%, almost full capacity = 75%–99%, and full capacity = 100% of the activity, knowledge, or resources described within the question were met.

TABLE. Level of education or training of food safety epidemiologists, by level of government — United States, 2010*

Level of education/training†	State		Region/District		Local		Total		FTEs needed to reach full capacity	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(% increase)
Doctoral degree	14.0	(6)	7.5	(4)	8.5	(2)	30.0	(4)	25.5	(85)
Professional background	25.5	(11)	9.0	(5)	18.0	(5)	52.5	(7)	28.0	(53)
Master's degree	93.5	(39)	54.0	(32)	60.5	(16)	208.0	(26)	152.5	(73)
Bachelor's degree	15.5	(6)	11.0	(7)	13.0	(3)	39.5	(5)	26.0	(66)
Nursing degree	29.0	(12)	37.0	(22)	151.0	(40)	217.0	(28)	47.5	(22)
Some coursework	25.0	(10)	11.5	(7)	33.0	(9)	69.5	(9)	14.0	(20)
On-the-job training	23.5	(10)	29.0	(17)	44.0	(12)	96.5	(12)	10.5	(11)
No formal training in epidemiology	14.0	(6)	10.0	(6)	50.0	(13)	74.0	(9)	0.0	—
Total	240.0	(100)	169.0	(100)	378.0	(100)	787.0	(100)	304.0	(38)

Abbreviation: FTE = full-time equivalent employee.

* Based on responses to an April 2010 web-based survey of state health departments by the Council of State and Territorial Epidemiologists.

† Doctoral degree = PhD, DrPH, or other doctoral degree in epidemiology; professional background = MD, DO, DVM, or DDS with a dual degree in epidemiology; master's degree = MPH, MSPH, MS, or other master's degree in epidemiology; bachelor's degree = BA, BS, or other bachelor's degree in epidemiology; nursing degree = RN, BSN, or other nursing designation; some coursework = completion of some coursework in epidemiology; on-the-job training = receipt of any type of on-the-job training in epidemiology.

(16% of states), *Listeria* (13%), *E. coli* (10%), norovirus (7%) and *Salmonella* (4%) (Figure 1).

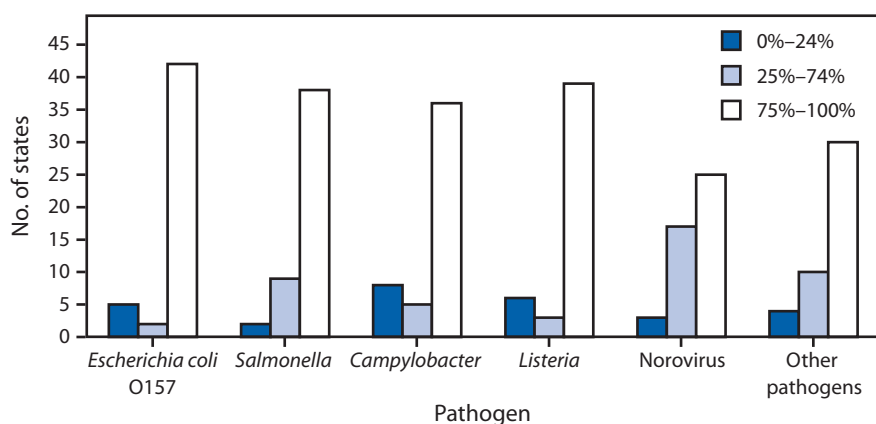
States were more likely to obtain stool specimens than food samples as part of foodborne outbreak investigations. Relatively few states reported always collecting either stool specimens (five states) or food (one state) samples associated with foodborne disease outbreaks; 33 states collected stool specimens in 50%–99% of outbreaks, and 36 states collected food samples in <50% of outbreaks. Thirty-nine states reported having performed 1–10 tracebacks of commercial products during the past 3 years; relatively few (seven states) had conducted ≥11 tracebacks, and three states completed no tracebacks of commercial products during that period.

All respondents reported barriers to investigating foodborne or enteric outbreaks. Barriers reported as either moderate or substantial by states included delayed notification of the

outbreak (reported by 41 states), lack of sufficient number of foodborne safety staff members (29), lower prioritization of investigations (27), lack of ability to pay overtime (20), lack of adequate epidemiology expertise (12), difficulties working with in-state agencies (eight), constraints related to administrative support (eight), and difficulties working with other state or federal agencies (five) (Figure 2).

In 2009, the Council to Improve Foodborne Outbreak Response (CIFOR) distributed to all states its *Guidelines for Foodborne Disease Outbreak Response* (5), which was intended to improve outbreak response. Among the states, 47 plan to read the document, 39 plan to distribute it, and 29 plan to review their practices against the recommendations in the *Guidelines* and the performance indicators therein. Few states reported plans to implement or incorporate the *Guidelines* into practice in the immediate future (27%).

FIGURE 1. Number of states investigating outbreaks of specific pathogens by proportion of outbreaks investigated — United States, 2010



* Based on responses to an April 2010 web-based survey of state health departments by the Council of State and Territorial Epidemiologists.

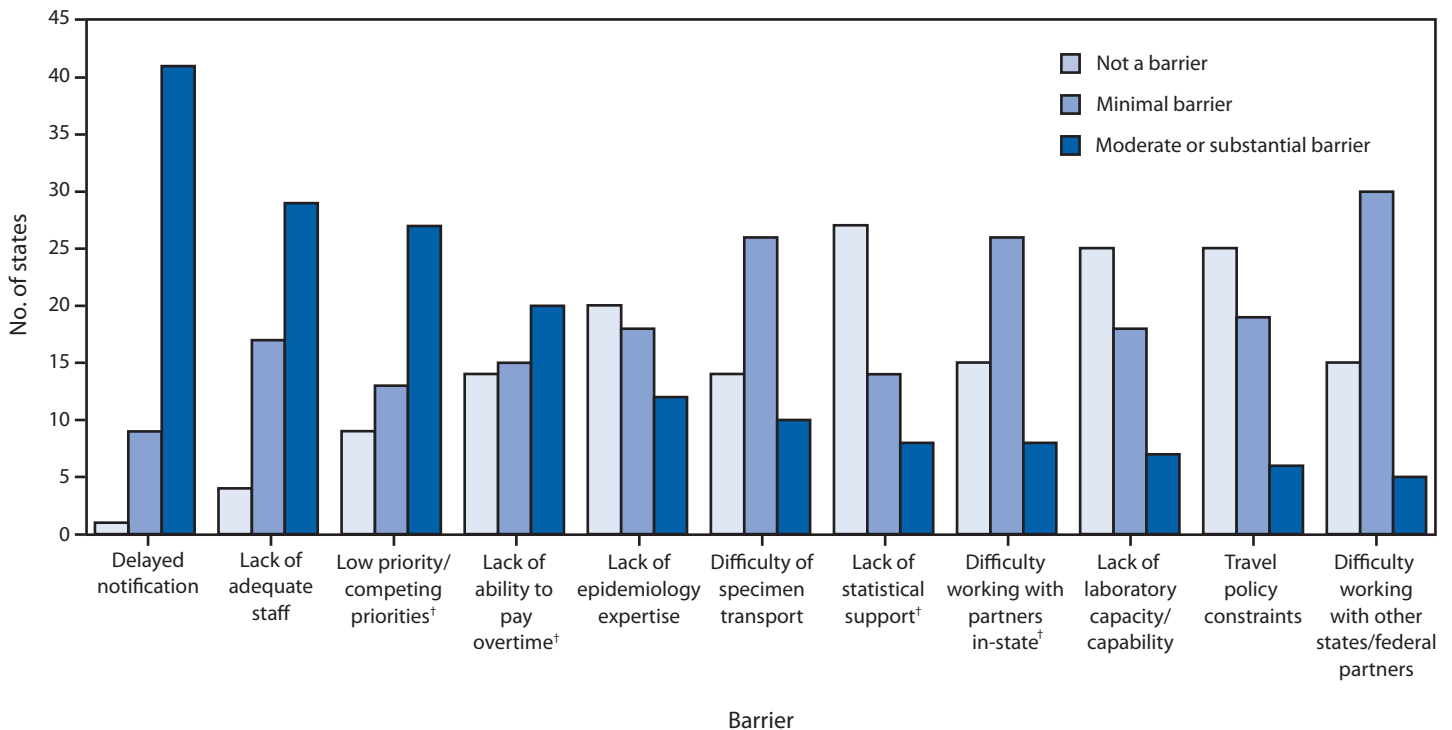
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Editorial Note

Ensuring adequate epidemiology capacity in foodborne disease programs is essential for the timely detection, investigation, control, and prevention of foodborne disease outbreaks. Although national foodborne disease

FIGURE 2. Number of states reporting selected barriers to investigation of enteric illness outbreaks during the past 3 years — United States, 2010*



* Based on responses to an April 2010 web-based survey of state health departments by the Council of State and Territorial Epidemiologists.

[†] Response = 49 states; response to all other barrier questions = 50 states.

epidemiology and surveillance capacity has increased since the previous CSTE assessment (1), critical gaps remain. Levels of formal epidemiology education among foodborne disease epidemiologists, especially at the local level, were lower than those of the national epidemiology workforce. Foodborne diseases personnel at the local level, compared with those at state and regional/district levels, were less likely to have an epidemiology degree and more likely to have only on-the-job-training or no formal training in epidemiology (6,7); previous assessments show this to be particularly true of nurses working as epidemiologists (8). States have a substantial need for additional FTEs, especially those with a master's degree in epidemiology, to reach full capacity in foodborne diseases program capacity at the state, local, and regional/district levels. Many of the specific activities assessed in this study directly rely on having enough trained or competent personnel on hand to perform them (e.g., conducting commercial tracebacks and collection of stool and food specimens). Insufficient workforce capacity hinders the ability to conduct these activities and, therefore, reduces the quality and quantity of foodborne investigations carried out by states.

Widespread use of electronic surveillance systems by states has increased the desirability and feasibility of electronic laboratory-based reporting and the potential for improving

the timeliness of infectious disease reporting and response. However, improvement and investment in public health IT infrastructure is needed to respond adequately to foodborne disease outbreaks. Improvements have resulted from several years of federal preparedness funding targeting states' development of electronic surveillance and reporting systems. Despite these improvements, many states report that they lack core capacity, which has directly affected their ability to investigate and control outbreaks of foodborne diseases and enteric illnesses. Data elements considered essential to routine surveillance for foodborne diseases are collected inconsistently across states and some, such as food purchasing locale, are collected by few. States also lack adequate IT infrastructure, based on their reported lack of timely notification as the single most common barrier to completion of foodborne disease investigations.

The findings in this report are subject to at least two limitations. First, state-level epidemiologists estimated current epidemiology capacity at regional/district and local levels. The methods used by responding states to estimate their own capacity were subjective and likely varied. Second, not all responding states answered every question. However, these findings still provide useful insight into foodborne disease epidemiology capacity at state and local levels.

References

What is already known on this topic?

Ensuring the safety of the food supply has become a national public health priority, and considerable resources at the federal, state, and local government levels have been directed at improving national food safety capacity.

What is added by this report?

Data from this assessment indicate that overall foodborne disease epidemiology capacity needs to improve to achieve full capacity to detect, investigate, and respond to foodborne disease outbreaks.

What are the implications for public health practice?

Agencies at the federal, state, and local levels should work together to improve capacity through increased staffing levels, enhanced training opportunities, and increased investment in health information technology.

CSTE recommends an increase in the number of personnel working in foodborne disease epidemiology and surveillance in state and local health departments, and enhanced training opportunities, including use of the CSTE/CDC applied epidemiology competencies (6) and the CIFOR *Guidelines for Foodborne Disease Outbreak Response* (5). Increased investment in IT also is needed to realize greater improvements in foodborne disease outbreak capacity.

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Recommendations on the Use of Quadrivalent Human Papillomavirus Vaccine in Males — Advisory Committee on Immunization Practices (ACIP), 2011

On October 25, 2011, the Advisory Committee on Immunization Practices (ACIP) recommended routine use of quadrivalent human papillomavirus (HPV) vaccine (HPV4; Gardasil, Merck & Co. Inc.) in males aged 11 or 12 years. ACIP also recommended vaccination with HPV4 for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated. These recommendations replace the October 2009 ACIP guidance that HPV4 may be given to males aged 9 through 26 years (1). For these recommendations, ACIP considered information on vaccine efficacy (including data available since October 2009, on prevention of grade 2 or 3 anal intraepithelial neoplasia [AIN2/3], a precursor of anal cancer), vaccine safety, estimates of disease and cancer resulting from HPV, cost-effectiveness, and programmatic considerations. The evidence for HPV4 vaccination of males was evaluated using Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methods (2).

Background of HPV Vaccination Program in the United States

HPV4 is directed against HPV types 6, 11, 16, and 18, and was licensed by the Food and Drug Administration (FDA) for use in females in June 2006. Bivalent HPV vaccine (HPV2; Cervarix, GlaxoSmithKline) is directed against HPV 16 and 18, and was licensed for use in females in October 2009. ACIP recommends either vaccine for routine use in females aged 11 or 12 years (3). In 2009, HPV4 was licensed for use in males for prevention of genital warts; in December 2010, FDA added prevention of anal cancer in males and females as an indication for use (4). Since 2006, HPV vaccine coverage in females has increased but remains low. In 2010, coverage with at least 1 dose among females aged 13 through 17 years was 48.7%, and 3-dose coverage was 32.0% (5). Coverage with at least 1 dose among males aged 13 through 17 years was <2%.

Burden of Disease and Cancer in Males

HPV-associated cancers in males include some anal, penile, and oropharyngeal cancers caused primarily by HPV 16 (6–9). An estimated 22,000 HPV 16- and 18-associated cancers occur annually in the United States, including an estimated 7,000 HPV 16- and 18-associated cancers in males (9). Data from U.S. cancer registries have shown increases in the incidence of oropharyngeal and anal cancers in men (8,9); an evaluation of data from 1973–2007 found increases of 1% per year for oropharyngeal cancers and 3% per year for anal cancers (9).

Nononcogenic HPV types, primarily 6 and 11, cause >90% of genital warts (condylomata) and most cases of recurrent respiratory papillomatosis. Approximately 250,000 cases of genital warts occur each year in the United States among sexually active males (10,11).

Efficacy

In a phase III efficacy trial, HPV4 had high efficacy for prevention of genital warts among 4,055 males aged 16 through 26 years. Exclusion criteria included history of genital warts, history of genital lesions possibly HPV-related, and less than one or more than five lifetime sex partners. Among those who received all 3 vaccine doses and were seronegative at day 1 and DNA-negative day 1 through month 7 to the respective HPV type (per protocol population), efficacy for prevention of HPV 6-, 11-, 16-, and 18-related genital warts was 89.3% (95% confidence interval [CI] = 65.3%–97.9%); efficacy for HPV 6- and 11-related genital warts was similar. Efficacy for prevention of HPV 6-, 11-, 16- and 18-related genital warts among males who received at least 1 vaccine dose, regardless of baseline infection or serology (intent to treat population), was 68.1% (CI = 48.8%–80.7%) (4). No efficacy was observed among males who were infected with the respective HPV type at baseline. Although grade 1, 2, and 3 penile/perineal/perianal intraepithelial neoplasias were evaluated, too few were observed, and efficacy was not demonstrated (4).

A substudy of the phase III efficacy trial included 598 men who have sex with men (MSM), aged 16 through 26 years; outcomes were genital warts; AIN grades 1, 2, or 3 (AIN1/2/3); and AIN2/3. Per protocol efficacy for prevention of HPV 6-, 11-, 16-, and 18-related genital warts was 88.1% (CI = 13.9%–99.7%) (Carlos Sattler, MD, Merck, personal communication, August 2011). Per protocol efficacy for prevention of HPV 6-, 11-, 16-, 18- related AIN1/2/3 was 77.5% (CI = 39.6%–93.3%), and against AIN2/3 was 74.9% (CI = 8.8%–95.4%) (Table) (4). In the intent to treat population, efficacy for prevention of HPV 6-, 11-, 16-, and 18-related AIN1/2/3 was 50.3% (CI = 25.7%–67.2%), and prevention of HPV 6-, 11-, 16-, and 18-related AIN2/3 was 54.2% (CI = 18.0%–75.3%) (4). In the intent to treat population, efficacy for prevention of any HPV type-related AIN2/3 was 24.3% (CI = -13.8%–50.0%) (4). No studies have evaluated the efficacy of HPV4 for prevention of recurrent respiratory papillomatosis or oropharyngeal cancer.

The efficacy of HPV4 for prevention of HPV-related precancerous lesions and disease is supported further by studies

TABLE. Efficacy of quadrivalent HPV vaccine for prevention of HPV 6-, 11-, 16-, and 18-related genital warts, AIN1/2/3, or AIN 2/3, per protocol,* in males aged 16 through 26 years[†]

Condition	Control		Vaccine		Vaccine efficacy	
	No.	Cases	No.	Cases	%	(95% CI)
Genital warts	1,404	28	1,394	3	89.3	(65.3–97.9)
AIN1/2/3 [§]	208	24	194	5	77.5	(39.6–93.3)
AIN2/3 [§]	208	13	194	3	74.9	(8.8–95.4)

Abbreviations: HPV = human papillomavirus; AIN = anal intraepithelial neoplasia; CI = confidence interval.

Source: Food and Drug Administration. Highlights of prescribing information. Gardasil (human papillomavirus quadrivalent [types 6, 11, 16 and 18]). Available at <http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm111263.pdf>.

* Per protocol population included males who received all 3 vaccine doses, were seronegative at day 1 and DNA negative at day 1 through month 7 to the respective HPV type, with case counting beginning after month 7.

[†] Participants were enrolled from North America, South America, Europe, Australia, and Asia; median duration of follow-up was 2.3 years for the study in all males and 2.6 years for the study in men who have sex with men (MSM).

[§] Efficacy for AIN studied in MSM.

among females. In three trials, HPV4 had high efficacy (>98%) for prevention of HPV 6-, 11-, 16-, and 18-related grade 2 or 3 cervical intraepithelial neoplasia (CIN2/3) or adenocarcinoma in situ (AIS), grade 2 or 3 vulvar intraepithelial neoplasia (VIN2/3), and grade 2 or 3 vaginal intraepithelial neoplasia (VaIN2/3) (12).

Immunogenicity

Data on immunogenicity in males are available from the phase III trial conducted among males aged 16 through 26 years and from bridging immunogenicity studies conducted among males aged 9 through 15 years (4). Seroconversion was high for all four HPV vaccine types and postvaccination antibody titers were significantly higher in males aged 9 through 15 years compared with males aged 16 through 26 years (4). Data from a follow-up study of 500 boys who were in an immunogenicity study showed no cases of persistent infection or disease related to any of the four HPV vaccine types during 6 years of follow-up (13). The high efficacy found in the clinical trials in females and males to date has not allowed identification of a minimum protective antibody titer.

Safety

Clinical trial data in approximately 5,300 males found that the most common adverse events were mild or moderate, and were most commonly injection-site reactions (4). Headache and fever were the most commonly reported systemic adverse events in vaccine recipients and controls (4). Since licensure, at least 40 million doses of HPV4 have been distributed in the United States through September 2011. National postlicensure safety data indicate that HPV4 adverse events were similar to those from prelicensure trials (14). Postlicensure safety data from the Vaccine Safety Datalink study, including data from >600,000 HPV4 doses administered, showed no statistically significant increased risk for the outcomes studied, including Guillain-Barré syndrome, stroke, venous thromboembolism,

appendicitis, seizures, syncope, allergic reactions, and anaphylaxis (15). Postlicensure safety data from a manufacturer-sponsored study found no increased risk for outcomes such as anaphylaxis and venous thromboembolism; however, persons who were vaccinated with HPV4 were more likely to faint on the day they were vaccinated than another period in which vaccine was not administered (16). ACIP recommends that vaccination providers should consider observing patients for 15 minutes after all vaccinations, including HPV vaccination.

Cost-Effectiveness

The cost-effectiveness* of male vaccination is sensitive to a range of assumptions, such as vaccine efficacy, vaccine coverage of females, the range of health outcomes included, and the effect of HPV-associated diseases on quality of life (17–20). Adding male vaccination to female-only vaccination becomes more cost-effective when all HPV-associated health outcomes are included in the model and vaccine coverage of females is low (e.g., 3-dose vaccine coverage <50% by age 12 years). Adding male vaccination to female-only vaccination becomes less cost-effective when considering scenarios such as only the health outcomes for which evidence of vaccine efficacy is available, when vaccine coverage of females is high (such as 3-dose vaccine coverage >70% by age 12 years), if vaccinated males have mostly vaccinated sex partners, and when male vaccination is compared with a strategy of increased vaccine coverage of females (20). At the current vaccine price, adding male vaccination at age 12 years to a female-only vaccination

* By charter, when considering recommendations for use of a vaccine, ACIP members' deliberations should include consideration of vaccine efficacy, as well as cost-benefit and risk-benefit analyses. No predefined threshold for cost-effectiveness is considered. To ensure that economic data presented to ACIP and its working groups are uniform in presentation, understandable, and of the highest quality, lead economists and the Health Economics Research Group at CDC developed *Guidance for Health Economics Studies Presented to the ACIP*, available at <http://www.cdc.gov/vaccines/recs/acip/economic-studies.htm>. The guidance specifically mandates technical review of any economic study that is presented to ACIP.

strategy would cost approximately \$20,000–\$40,000 per quality-adjusted life year (QALY) in the more favorable scenarios and approximately \$75,000 to >\$250,000 per QALY in less favorable scenarios (18–20). Vaccination of adult males becomes less cost-effective as age at vaccination increases, and models suggest the cost per QALY gained by vaccinating males >21 years would be approximately 2–4 times that of vaccinating males aged <18 years (21).

Special Populations

MSM are at higher risk for conditions associated with HPV types 6, 11, 16, and 18 than are heterosexual men; diseases and cancers that have a higher incidence among MSM include AIN, anal cancers, and genital warts (22,23). HPV4 clinical trial data demonstrated high efficacy for prevention of genital warts, AIN1/2/3, and AIN2/3 (4). HPV4 is not licensed for males aged >26 years, and no information is available on the efficacy for prevention of outcomes in MSM aged >26 years. A cost-effectiveness analysis estimated <\$50,000 per QALY for vaccination of MSM through age 26 years, using various assumptions (24).

Persons infected with the human immunodeficiency virus (HIV) also have a high burden of HPV-associated outcomes. Genital warts are more common and more difficult to treat in HIV-infected persons (25). AIN and anal cancer are common in HIV-infected MSM, and data suggest that effective antiretroviral therapy has not reduced the burden of anal cancer (26). One small trial in HIV-infected boys and girls found HPV4 to be safe and immunogenic (27), as did a study in HIV-infected men (28). Antibody titers to vaccine types 6 and 18 were lower in HIV-infected children than those observed in age-matched HIV-uninfected children; the clinical significance of this is not known (27). Ongoing studies will evaluate the efficacy and duration of immune response in HIV-infected persons.

GRADE

Data on HPV4 for males were reviewed according to GRADE methods (2). Factors considered in determining the recommendation included benefits and harms, evidence type, values and preferences, and health economic analysis.[†]

Rationale

Although the largest number of HPV-associated cancers occur in women (approximately 15,000 HPV 16- and 18-associated cancers each year), an estimated 7,000 HPV 16- and 18-associated cancers occur each year in men in the United States. These include anal, oropharyngeal, and penile

cancers. HPV4 has high efficacy for prevention of genital warts, AIN1/2/3, and AIN2/3 in males. HPV4 also has high efficacy for prevention of genital warts, CIN1/2/3 or AIS, CIN2/3, VIN2/3, and VaIN2/3 in females. Although data show HPV4 prevents various outcomes, no data are available on the efficacy for prevention of oropharyngeal or penile cancers. Vaccination of males would provide direct benefits and likely would reduce HPV 6, 11, 16, and 18 transmission, and resulting infection, disease, and cancers in females (through herd immunity). However, no clinical efficacy data demonstrating that HPV4 prevents HPV transmission are available.

Because HPV4 is prophylactic, it would be most effective when given before exposure to HPV through sexual contact. The recommendation for vaccination at ages 11 or 12 years is supported by data from the efficacy trial, demonstrating highest efficacy in males who had no evidence of previous or current HPV vaccine type infection, data on sexual behavior in the United States, and immunogenicity studies showing higher antibody titers after vaccination of males at ages 9 through 15 years compared with those aged 16 through 26 years. Other vaccines are recommended at age 11 or 12 years, including HPV vaccine for females. The population level benefits decrease with increasing age at vaccination, especially after age 21 years.

Recommendations

ACIP recommends routine vaccination of males aged 11 or 12 years with HPV4 administered as a 3-dose series (recommendation category: A, evidence type: 2[§]). The vaccination series can be started beginning at age 9 years. Vaccination with HPV4 is recommended for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series. Males aged 22 through 26 years may be vaccinated. Recommendations for administration and precautions are unchanged from previous recommendations (1).

Recommendations for Special Populations

HPV4 is not a live vaccine and can be administered to persons who are immunocompromised as a result of infection (including HIV), disease, or medications. The immune response and vaccine efficacy might be less than that in immunocompetent persons. For immunocompromised males, ACIP recommends routine vaccination with HPV4 as for all males, and vaccination through age 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series.

[†] Additional information is available at <http://www.cdc.gov/vaccines/recs/acip/grade/table-refs.htm>.

[§] Recommendation category A: recommendation that applies to all persons in an age or risk-based group. Evidence type 2: randomized controlled trials with important limitations or exceptionally strong evidence from observational studies.

MSM are at higher risk for infection with HPV types 6, 11, 16, and 18 and associated conditions, including genital warts and anal cancer. For MSM, ACIP recommends routine vaccination with HPV4 as for all males, and vaccination through age 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series.

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Use of Hepatitis B Vaccination for Adults with Diabetes Mellitus: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Hepatitis B virus (HBV) causes acute and chronic infection of the liver leading to substantial morbidity and mortality. In the United States, since 1996, a total of 29 outbreaks of HBV infection in one or multiple long-term-care (LTC) facilities, including nursing homes and assisted-living facilities, were reported to CDC; of these, 25 involved adults with diabetes receiving assisted blood glucose monitoring (1; CDC, unpublished data, 2011). These outbreaks prompted the Hepatitis Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) to evaluate the risk for HBV infection among all adults with diagnosed diabetes. The Work Group reviewed HBV infection-related morbidity and mortality and the effectiveness of implementing infection prevention and control measures. The strength of scientific evidence regarding protection was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology,* and safety, values, and cost-effectiveness were incorporated into a recommendation using the GRADE system. Based on the Work Group findings, on October 25, 2011, ACIP recommended that all previously unvaccinated adults aged 19 through 59 years with diabetes mellitus (type 1 and type 2) be vaccinated against hepatitis B as soon as possible after a diagnosis of diabetes is made (recommendation category A). Data on the risk for hepatitis B among adults aged ≥ 60 years are less robust. Therefore, ACIP recommended that unvaccinated adults aged ≥ 60 years with diabetes may be vaccinated at the discretion of the treating clinician after assessing their risk and the likelihood of an adequate immune response to vaccination (recommendation category B). This report summarizes these recommendations and provides the rationale used by ACIP to inform their decision making.

Risk for HBV Infection

An estimate of the risk for HBV infection for adults with diabetes living in LTC facilities was not available; continuing outbreaks suggest that it might be substantial. The population

* *Recommendation category A*: a recommendation that applies to all persons in an age or risk-based group. *Recommendation category B*: a recommendation for individual clinical decision making. *Evidence type 1*: randomized controlled trials, or overwhelming evidence from observational studies. *Evidence type 2*: randomized controlled trials with important limitations, or exceptionally strong evidence from observational studies. *Evidence type 3*: observational studies, or randomized controlled trials with notable limitations. *Evidence type 4*: clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations. **Source**: Ahmed F, Temte JL, Campos-Outcalt D, Schünemann HJ; for the ACIP Evidence Based Recommendations Work Group (EBRWG). Methods for developing evidence-based recommendations by the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (CDC). *Vaccine* 2011;29:9171–6. Additional information about the GRADE methodology related to this policy is available at <http://www.cdc.gov/vaccines/rct/acip/grade/table-refs.htm>.

risk for HBV infection among adults with diagnosed diabetes was estimated from 865 confirmed cases of acute HBV infection reported during 2009–2010 from eight Emerging Infections Program (EIP) sites constituting approximately 17% of the U.S. population. The analysis was restricted to persons aged ≥ 23 years because of high rates of vaccination among younger persons. In multivariate analyses that considered persons without hepatitis B-related risk behaviors (i.e., injection-drug use, male sex with a male, and sex with multiple partners), persons aged 23 through 59 years with diabetes had 2.1 (95% confidence interval [CI] = 1.6–2.8) times the odds of developing acute hepatitis B as those without diabetes; the odds were 1.5 (CI = 0.9–2.5) times as likely for persons aged ≥ 60 years. The annual incidence of reported cases of acute HBV infection among adults with diabetes was 1.8 per 100,000 (CI = 1.5–2.2) (2). Acute HBV infection incidence is underestimated; an additional 10.5 new cases of infection likely occurred for each reported, confirmed case (3).

Data for the period 1999–2010 from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the noninstitutionalized U.S. population, indicated a 60% ($p < 0.001$) higher seroprevalence of antibody to hepatitis B core antigen (indicative of past or present HBV infection) overall among persons aged ≥ 18 years with diagnosed diabetes compared with those without diabetes. Stratified by age, the estimated prevalence ratios were 1.7 (CI = 1.3–2.2) for persons aged 18 through 59 years and 1.3 (CI = 1.0–1.6) for those aged ≥ 60 years (CDC, unpublished data, 2011).

Morbidity and Mortality

The severity of acute HBV infection among adults ranges from asymptomatic to fulminant hepatitis. National viral hepatitis surveillance data indicate that of the 3,371 acute HBV infections reported in 2009, 47% of the 2,126 infections for which information was available resulted in hospitalization, and 1% of the 1,900 infections for which information was available were fatal (3). Data from EIP for the period 2009–2010 indicated a higher case-fatality rate among acute HBV-infected persons with diagnosed diabetes compared with those without diabetes, although the difference was not statistically significant (5% versus 2%, $p = 0.127$) (2). Acute HBV infection progresses to chronic infection in approximately 5% of otherwise healthy adults (4), but is believed to be greater among older adults with diabetes (5). In the United States, an estimated 700,000 to 1.4 million persons are infected with HBV (3). Because chronic HBV infection can persist for decades, persons with chronic HBV infection are the

reservoir for continuing HBV transmission. Chronic HBV infection is associated with high morbidity and mortality, leading to cirrhosis and liver cancer in $\geq 15\%$ of affected adults (5).

Diabetes is associated with nonalcoholic fatty liver disease, including its most severe form, nonalcoholic steatohepatitis. A study of veterans without HBV infection indicated that adults with diabetes have approximately twice the risk for chronic nonalcoholic liver disease and hepatocellular carcinoma as those without diabetes (6).

Infection Control

HBV is highly infectious and environmentally stable (5); HBV can be transmitted by medical equipment that is contaminated with blood that is not visible to the unaided eye. Percutaneous exposures to HBV occur as a result of assisted monitoring of blood glucose (7) and other procedures involving instruments or parenteral treatments shared between persons. Lapses in infection control during assisted blood glucose monitoring that have led to HBV transmission include multipatient use of finger stick devices designed for single-patient use and inadequate disinfection and cleaning of blood glucose monitors between patients. Breaches have been documented in various settings, including LTC facilities, hospitals, community health centers, ambulatory surgical centers, private offices, homes, and health fairs (7; CDC, unpublished data, 2011). Initiatives are ongoing to encourage improvement in the design and labeling of devices used in diabetes monitoring and care, and for greater oversight and training of staff responsible for providing diabetes care.[†]

Infection control guidelines for safe blood glucose monitoring have been available since 1990, and guidelines targeting LTC settings were published in 2005 (8). Since 1982, hepatitis B vaccination has been recommended for health-care personnel, including personnel exposed to blood in LTC settings, in conjunction with meticulous attention to infection control practice (5,8). In addition, a recommendation for hepatitis B vaccination exists for persons beginning hemodialysis (5).

Hepatitis B Vaccine

Two single-antigen recombinant hepatitis B vaccines, Recombivax HB (Merck & Co., Inc.) and Engerix-B (GlaxoSmithKline Biologicals), and one combination hepatitis A and hepatitis B vaccine, Twinrix (GlaxoSmithKline Biologicals), are available in the United States. Hepatitis B vaccines have been used in the United States since 1982. Extensive data support their safety in all age groups (5).

Hepatitis B vaccination usually consists of 3 doses of vaccine administered intramuscularly at 0, 1, and 6 months; other schedules are available. At younger ages, the immune response to

vaccine is similar among adults with and without diabetes. The proportion of adults who achieve seroprotection (≥ 10 mIU/mL antibody to hepatitis B surface antigen [anti-HBs]) after receipt of the 3-dose vaccine series decreases with age, obesity, smoking, immunosuppression, and comorbid conditions including diabetes. When the antibody responses among older adults with and without diabetes are compared, the response might be reduced among those with diabetes. A synthesis of available literature suggests a protective response is achieved after completion of the hepatitis B vaccine series in $\geq 90\%$, 80%, 65%, and $<40\%$ of adults with diabetes lacking comorbid conditions aged ≤ 40 years, 41 through 59 years, 60 through 69 years, and ≥ 70 years, respectively (CDC, unpublished data, 2011). Revaccination with 1–3 additional doses of hepatitis B vaccine safely increases the proportion of adults who achieve a protective level of anti-HBs (≥ 10 mIU/mL) (5). The duration of protection against symptomatic and chronic HBV infection lasts >22 years among healthy vaccine responders (9); duration of immunity among persons with diabetes is unknown.

Cost-Effectiveness

The Hepatitis Vaccines Work Group developed economic models that yielded age-stratified calculations (base case) of the incremental cost per quality-adjusted life-year (QALY) saved based on vaccinating adults with diabetes against hepatitis B.[§] The estimated cost per QALY saved was \$75,100 for persons aged 20 through 59 years but increased substantially with increasing age. From a lifetime perspective, a one-time vaccination program consisting of a 3-dose series of hepatitis B vaccine, covering 10% of unvaccinated U.S. adults with diagnosed diabetes aged 20 through 59 years (or approximately 528,047 persons) would be expected to prevent 4271 HBV infections, 467 hospitalizations, 256 chronic cases, 33 cases of hepatocellular carcinoma, 13 liver transplants, and 130 deaths. Postvaccination serologic testing and revaccination would add considerable cost, with limited increase in disease protection (CDC, unpublished data, 2011).

ACIP Recommendations

On the basis of available information about HBV risk, morbidity and mortality, available vaccines, age at diagnosis of diabetes, and cost-effectiveness, ACIP recommends the following:

[§]The Charter of ACIP states that, when considering recommendations for use of a vaccine, ACIP members' deliberations should include consideration of vaccine efficacy as well as cost-benefit and risk-benefit analyses. No predefined threshold for cost-effectiveness is considered. To ensure that economic data presented to the Committee and its Working Groups are uniform in presentation, understandable, and of the highest quality, lead economists and the Health Economics Research Group at CDC developed *Guidance for Health Economics Studies Presented to the Advisory Committee on Immunization Practices (ACIP)*, available at <http://www.cdc.gov/vaccines/recs/acip/economic-studies.htm>. The guidance specifically mandates technical review of any economic study that is presented to ACIP.

[†]Additional information available at <http://www.cdc.gov/injectionsafety/meetings/stickingwsafety52010.html>.

- Hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A; evidence type 2).
- Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥ 60 years (recommendation category B; evidence type 2).

Remarks

Continued efforts are needed to increase adherence to recommended infection control practice. Shared use of blood-contaminated equipment increases the risk for exposure to bloodborne pathogens, including hepatitis C virus, human immunodeficiency virus, and HBV, which is highly infectious.

Administration of the hepatitis B vaccine series should be completed as soon as feasible after diabetes is diagnosed. Available data do not confirm an advantage to any specific hepatitis B vaccine, dosage, or approved schedule for adults with diabetes. No serologic testing or additional hepatitis B vaccination is recommended for adults who received a complete series of hepatitis B vaccinations at any time in the past.

The hepatitis B vaccination series can be given safely to persons of any age, but current hepatitis B vaccines are less efficacious and less cost-effective among older adults. Evidence for the extent of increased risk for acute HBV infection among persons with diabetes who are aged ≥ 60 years is less strong than for younger persons with diabetes. In 2008, the median age of diabetes diagnosis was 53 years; two thirds of adult diabetes diagnoses were made before age 60 years.[¶]

Decisions to vaccinate adults with diabetes who are aged ≥ 60 years of age should incorporate consideration of the patient's likelihood of acquiring HBV infection, including the risk posed by an increased need for assisted blood-glucose monitoring in LTC facilities, the likelihood of experiencing chronic sequelae if infected with HBV, and the declining immunologic responses to vaccines that are associated with frailty, a geriatric syndrome characterized by decreased physiologic reserve and increased vulnerability, leading to early mortality in older adults (10).

Hepatitis B vaccine may be administered during health-care visits scheduled for other purposes as long as minimum intervals between doses are observed; there is no maximum interval between doses that makes the hepatitis B vaccination series ineffective.

Reported by

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[¶]Additional information available at <http://www.cdc.gov/diabetes/statistics/age/fig1.htm>.

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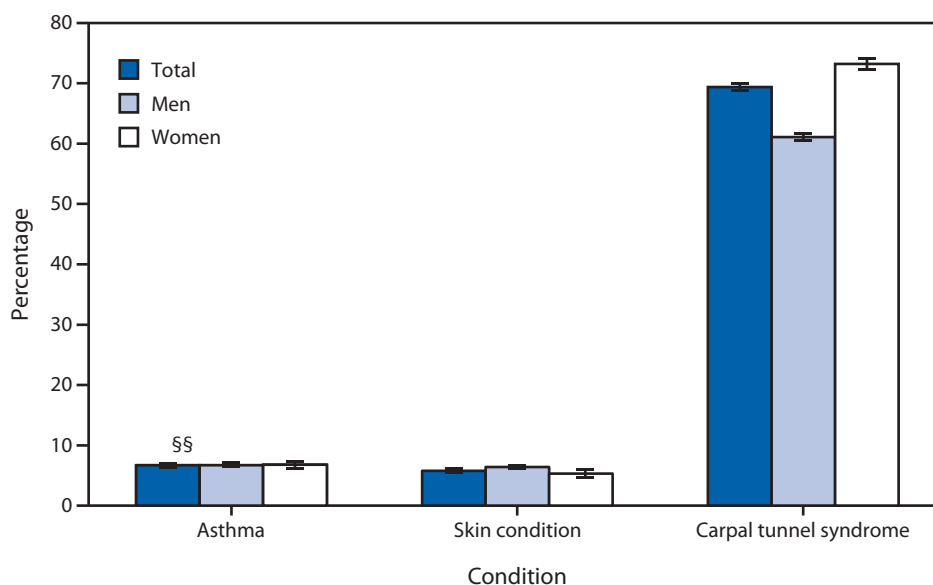
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Employed Adults* Aged 18–64 Years with Current Asthma,[†] Skin Condition,[§] or Carpal Tunnel Syndrome[¶] Who Were Told Their Condition Was Work-Related,** by Sex — National Health Interview Survey, 2010^{††}



* Employed adults are persons who had worked at a job or business any time in the 12 months before the interview (either full-time or part-time).

[†] Adults were defined as having current asthma if they answered “yes” to the following two questions: “Have you ever been told by a doctor or other health professional that you had asthma?” “Do you still have asthma?”

[§] Adults were defined as having a skin condition if they answered “yes” to the following question: “During the past 12 months, have you had dermatitis, eczema, or any other red, inflamed skin rash?”

[¶] Adults were defined as having carpal tunnel syndrome if they answered “yes” to the following two questions: “Have you ever been told by a doctor or other health professional that you have a condition affecting the wrist and hand called carpal tunnel syndrome?” and “During the past 12 months, have you had carpal tunnel syndrome?”

** Asthma was considered work-related if a doctor or other health professional had told the adult that it “was probably caused by your work,” “was probably made worse by your work,” or “was ever made worse by any job you have ever had.” Skin condition and carpal tunnel syndrome were considered work-related if a doctor or other health professional had told the adult that the condition “was probably work-related.”

^{††} Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey sample adult component. Asthma, skin condition, and carpal tunnel syndrome were the only three conditions for which participants were asked if a doctor or health professional had told them the condition was probably work-related.

§§ 95% confidence interval.

In 2010, among employed adults aged 18–64 years who currently had asthma, 6.7% had been told their current asthma was work-related. Among employed adults who had a skin condition, 5.8% had been told their skin condition was work-related. Among employed adults who had carpal tunnel syndrome, 69.4% had been told their carpal tunnel syndrome was work-related. Men (61.1%) were less likely than women (73.2%) to have been told their carpal tunnel syndrome was work-related. No significant differences by sex for either work-related current asthma or skin conditions were observed.

Source: National Health Interview Survey, 2010 data. Available at <http://www.cdc.gov/nchs/nhis.htm>.

Notifiable Diseases and Mortality Tables

TABLE I. Provisional cases of infrequently reported notifiable diseases (<1,000 cases reported during the preceding year) — United States, week ending December 17, 2011 (50th week)*

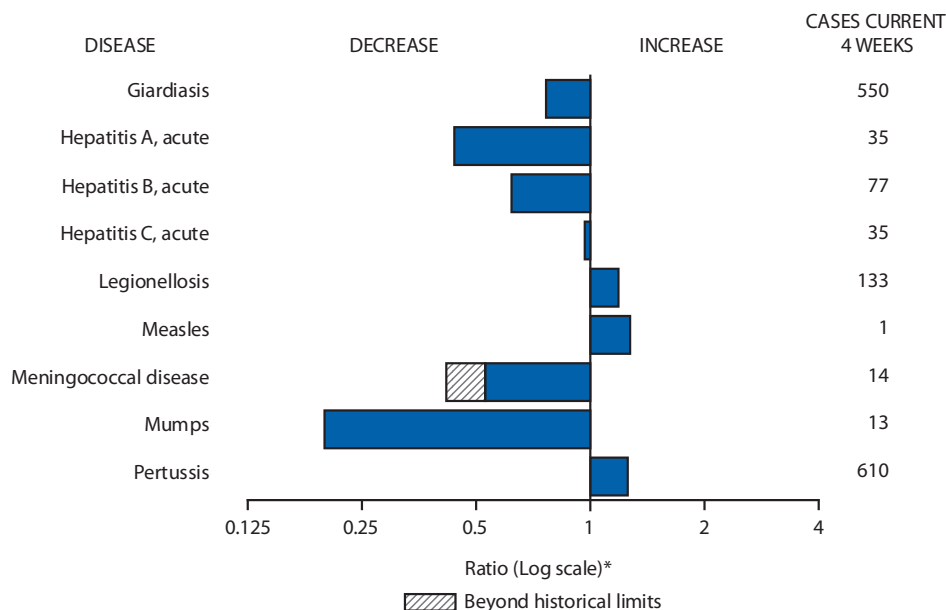
Disease	Current week	Cum 2011	5-year weekly average [†]	Total cases reported for previous years					States reporting cases during current week (No.)
				2010	2009	2008	2007	2006	
Anthrax	—	1	0	—	1	—	1	1	
Arboviral diseases ^{§, ¶} :									
California serogroup virus disease	—	125	0	75	55	62	55	67	
Eastern equine encephalitis virus disease	—	4	—	10	4	4	4	8	
Powassan virus disease	—	14	0	8	6	2	7	1	
St. Louis encephalitis virus disease	—	5	0	10	12	13	9	10	
Western equine encephalitis virus disease	—	—	—	—	—	—	—	—	
Babesiosis	2	622	0	NN	NN	NN	NN	NN	NY (2)
Botulism, total	1	106	4	112	118	145	144	165	
foodborne	—	8	1	7	10	17	32	20	
infant	1	68	3	80	83	109	85	97	NV (1)
other (wound and unspecified)	—	30	1	25	25	19	27	48	
Brucellosis	—	75	3	115	115	80	131	121	
Chancroid	—	27	1	24	28	25	23	33	
Cholera	—	29	0	13	10	5	7	9	
Cyclosporiasis [§]	1	140	1	179	141	139	93	137	FL (1)
Diphtheria	—	—	—	—	—	—	—	—	
<i>Haemophilus influenzae</i> ,** invasive disease (age <5 yrs):									
serotype b	—	7	1	23	35	30	22	29	
nonsensory type b	—	102	6	200	236	244	199	175	
unknown serotype	4	226	5	223	178	163	180	179	PA (2), OH (1), MO (1)
Hansen disease [§]	2	48	1	98	103	80	101	66	FL (2)
Hantavirus pulmonary syndrome [§]	—	20	1	20	20	18	32	40	
Hemolytic uremic syndrome, postdiarrheal [§]	—	200	7	266	242	330	292	288	
Influenza-associated pediatric mortality ^{§, ††}	—	118	2	61	358	90	77	43	
Listeriosis	8	729	19	821	851	759	808	884	NY (2), PA (2), FL (1), WA (1), CA (2)
Measles ^{§§}	—	210	1	63	71	140	43	55	
Meningococcal disease, invasive ^{¶¶} :									
A, C, Y, and W-135	—	175	8	280	301	330	325	318	
serogroup B	—	99	5	135	174	188	167	193	
other serogroup	—	12	0	12	23	38	35	32	
unknown serogroup	2	357	12	406	482	616	550	651	TN (1), CO (1)
Novel influenza A virus infections ^{***}	—	8	0	4	43,774	2	4	NN	
Plague	—	2	—	2	8	3	7	17	
Polio myelitis, paralytic	—	—	0	—	1	—	—	—	
Polio virus Infection, nonparalytic [§]	—	—	—	—	—	—	—	NN	
Psittacosis [§]	—	2	0	4	9	8	12	21	
Q fever, total [§]	2	104	3	131	113	120	171	169	
acute	1	77	2	106	93	106	—	—	TX (1)
chronic	1	27	1	25	20	14	—	—	TX (1)
Rabies, human	—	2	0	2	4	2	1	3	
Rubella ^{†††}	—	5	0	5	3	16	12	11	
Rubella, congenital syndrome	—	—	—	—	2	—	—	1	
SARS-CoV [§]	—	—	—	—	—	—	—	—	
Smallpox [§]	—	—	—	—	—	—	—	—	
Streptococcal toxic-shock syndrome [§]	4	106	4	142	161	157	132	125	NY (2), NC (2)
Syphilis, congenital (age <1 yr) ^{§§§}	—	229	8	377	423	431	430	349	
Tetanus	—	9	1	26	18	19	28	41	
Toxic-shock syndrome (staphylococcal) [§]	—	69	2	82	74	71	92	101	
Trichinellosis	—	9	0	7	13	39	5	15	
Tularemia	—	136	2	124	93	123	137	95	
Typhoid fever	—	305	9	467	397	449	434	353	
Vancomycin-intermediate <i>Staphylococcus aureus</i> [§]	—	61	1	91	78	63	37	6	
Vancomycin-resistant <i>Staphylococcus aureus</i> [§]	—	—	0	2	1	—	2	1	
Vibriosis (noncholera <i>Vibrio</i> species infections) [§]	8	707	10	846	789	588	549	NN	FL (2), TX (1), AZ (1), CA (4)
Viral hemorrhagic fever ^{¶¶¶}	—	—	—	1	NN	NN	NN	NN	
Yellow fever	—	—	—	—	—	—	—	—	

See Table 1 footnotes on next page.

TABLE I. (Continued) Provisional cases of infrequently reported notifiable diseases (<1,000 cases reported during the preceding year) — United States, week ending December 17, 2011 (50th week)*

—: No reported cases. N: Not reportable. NN: Not Nationally Notifiable. Cum: Cumulative year-to-date counts.
 * Case counts for reporting year 2011 are provisional and subject to change. For further information on interpretation of these data, see http://www.cdc.gov/osels/ph_surveillance/nndss/phs/files/ProvisionalNationalNotifiableDiseasesSurveillanceData20100927.pdf.
 † Calculated by summing the incidence counts for the current week, the 2 weeks preceding the current week, and the 2 weeks following the current week, for a total of 5 preceding years. Additional information is available at http://www.cdc.gov/osels/ph_surveillance/nndss/phs/files/5yearweeklyaverage.pdf.
 ‡ Not reportable in all states. Data from states where the condition is not reportable are excluded from this table except starting in 2007 for the arboviral diseases, STD data, TB data, and influenza-associated pediatric mortality, and in 2003 for SARS-CoV. Reporting exceptions are available at http://www.cdc.gov/osels/ph_surveillance/nndss/phs/infdis.htm.
 ¶ Includes both neuroinvasive and nonneuroinvasive. Updated weekly from reports to the Division of Vector-Borne Infectious Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases (ArboNET Surveillance). Data for West Nile virus are available in Table II.
 ** Data for H. influenzae (all ages, all serotypes) are available in Table II.
 †† Updated weekly from reports to the Influenza Division, National Center for Immunization and Respiratory Diseases. Since October 2, 2011, no influenza-associated pediatric deaths occurring during the 2011-12 influenza season have been reported.
 ‡‡ No measles cases were reported for the current week.
 ¶¶ Data for meningococcal disease (all serogroups) are available in Table II.
 *** CDC discontinued reporting of individual confirmed and probable cases of 2009 pandemic influenza A (H1N1) virus infections on July 24, 2009. During 2009, four cases of human infection with novel influenza A viruses, different from the 2009 pandemic influenza A (H1N1) strain, were reported to CDC. The four cases of novel influenza A virus infection reported to CDC during 2010, and the eight cases reported during 2011, were identified as swine influenza A (H3N2) virus and are unrelated to the 2009 pandemic influenza A (H1N1) virus. Total case counts are provided by the Influenza Division, National Center for Immunization and Respiratory Diseases (NCIRD).
 ††† No rubella cases were reported for the current week.
 §§§ Updated weekly from reports to the Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention.
 ¶¶¶ There was one case of viral hemorrhagic fever reported during week 12 of 2010. The one case report was confirmed as lassa fever. See Table II for dengue hemorrhagic fever.

FIGURE I. Selected notifiable disease reports, United States, comparison of provisional 4-week totals December 17, 2011, with historical data



* Ratio of current 4-week total to mean of 15 4-week totals (from previous, comparable, and subsequent 4-week periods for the past 5 years). The point where the hatched area begins is based on the mean and two standard deviations of these 4-week totals.

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TABLE II. (Continued) Provisional cases of selected notifiable diseases, United States, weeks ending December 17, 2011, and December 18, 2010 (50th week)*

Reporting area	Dengue Virus Infection†									
	Dengue Fever§					Dengue Hemorrhagic Fever¶				
	Current week	Previous 52 weeks		Cum 2011	Cum 2010	Current week	Previous 52 weeks		Cum 2011	Cum 2010
	Med	Max				Med	Max			
United States	—	3	16	203	684	—	0	1	2	10
New England	—	0	1	2	10	—	0	0	—	—
Connecticut	—	0	0	—	—	—	0	0	—	—
Maine**	—	0	0	—	6	—	0	0	—	—
Massachusetts	—	0	0	—	—	—	0	0	—	—
New Hampshire	—	0	0	—	—	—	0	0	—	—
Rhode Island**	—	0	0	—	1	—	0	0	—	—
Vermont**	—	0	1	2	3	—	0	0	—	—
Mid. Atlantic	—	1	6	56	222	—	0	0	—	5
New Jersey	—	0	0	—	29	—	0	0	—	—
New York (Upstate)	—	0	1	—	31	—	0	0	—	2
New York City	—	0	4	40	141	—	0	0	—	3
Pennsylvania	—	0	2	16	21	—	0	0	—	—
E.N. Central	—	0	2	14	67	—	0	1	1	1
Illinois	—	0	2	4	21	—	0	1	1	—
Indiana	—	0	1	2	14	—	0	0	—	—
Michigan	—	0	1	2	9	—	0	0	—	—
Ohio	—	0	1	2	16	—	0	0	—	—
Wisconsin	—	0	2	4	7	—	0	0	—	1
W.N. Central	—	0	2	11	33	—	0	0	—	1
Iowa	—	0	1	3	2	—	0	0	—	—
Kansas	—	0	1	1	4	—	0	0	—	—
Minnesota	—	0	1	5	14	—	0	0	—	—
Missouri	—	0	1	1	5	—	0	0	—	—
Nebraska**	—	0	0	—	7	—	0	0	—	—
North Dakota	—	0	1	1	1	—	0	0	—	—
South Dakota	—	0	0	—	—	—	0	0	—	1
S. Atlantic	—	1	8	81	237	—	0	1	1	2
Delaware	—	0	2	2	—	—	0	0	—	—
District of Columbia	—	0	0	—	—	—	0	0	—	—
Florida	—	1	7	61	188	—	0	0	—	2
Georgia	—	0	1	3	12	—	0	0	—	—
Maryland**	—	0	2	5	—	—	0	0	—	—
North Carolina	—	0	1	2	8	—	0	0	—	—
South Carolina**	—	0	1	1	13	—	0	0	—	—
Virginia**	—	0	1	7	14	—	0	1	1	—
West Virginia	—	0	0	—	2	—	0	0	—	—
E.S. Central	—	0	3	8	7	—	0	0	—	—
Alabama**	—	0	1	2	4	—	0	0	—	—
Kentucky	—	0	1	3	2	—	0	0	—	—
Mississippi	—	0	0	—	—	—	0	0	—	—
Tennessee**	—	0	2	3	1	—	0	0	—	—
W.S. Central	—	0	2	9	28	—	0	0	—	1
Arkansas**	—	0	0	—	—	—	0	0	—	1
Louisiana	—	0	1	3	4	—	0	0	—	—
Oklahoma	—	0	0	—	5	—	0	0	—	—
Texas**	—	0	1	6	19	—	0	0	—	—
Mountain	—	0	1	4	24	—	0	0	—	—
Arizona	—	0	1	2	12	—	0	0	—	—
Colorado	—	0	0	—	—	—	0	0	—	—
Idaho**	—	0	0	—	3	—	0	0	—	—
Montana**	—	0	0	—	4	—	0	0	—	—
Nevada**	—	0	1	1	4	—	0	0	—	—
New Mexico**	—	0	0	—	1	—	0	0	—	—
Utah	—	0	1	1	—	—	0	0	—	—
Wyoming**	—	0	0	—	—	—	0	0	—	—
Pacific	—	0	4	18	56	—	0	0	—	—
Alaska	—	0	0	—	1	—	0	0	—	—
California	—	0	2	5	36	—	0	0	—	—
Hawaii	—	0	4	5	—	—	0	0	—	—
Oregon	—	0	0	—	—	—	0	0	—	—
Washington	—	0	1	8	19	—	0	0	—	—
Territories										
American Samoa	—	0	0	—	—	—	0	0	—	—
C.N.M.I.	—	—	—	—	—	—	—	—	—	—
Guam	—	0	0	—	—	—	0	0	—	—
Puerto Rico	—	23	82	1,361	10,586	—	0	3	30	237
U.S. Virgin Islands	—	0	0	—	—	—	0	0	—	—

C.N.M.I.: Commonwealth of Northern Mariana Islands.

U: Unavailable. —: No reported cases. N: Not reportable. NN: Not Nationally Notifiable. Cum: Cumulative year-to-date counts. Med: Median. Max: Maximum.

* Case counts for reporting year 2011 are provisional and subject to change. For further information on interpretation of these data, see http://www.cdc.gov/osels/ph_surveillance/nndss/phps/files/ProvisionalNationa%20NotifiableDiseasesSurveillanceData20100927.pdf. Data for TB are displayed in Table IV, which appears quarterly.

† Updated weekly from reports to the Division of Vector-Borne Infectious Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases (ArboNET Surveillance).

§ Dengue Fever includes cases that meet criteria for Dengue Fever with hemorrhage, other clinical and unknown case classifications.

¶ DHF includes cases that meet criteria for dengue shock syndrome (DSS), a more severe form of DHF.

** Contains data reported through the National Electronic Disease Surveillance System (NEDSS).

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