# Risk and Management of Blood-Borne Infections in Health Care Workers

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INTRODUCTION	
TRANSMISSION OF BLOOD-BORNE PATHOGENS IN THE HEALTH CARE SETTING	
Modes of Blood-Borne Pathogen Transmission	
Epidemiology of Blood Contact	
DETECTION AND DIAGNOSIS OF BLOOD-BORNE PATHOGEN INFECTIONS	
Detection and Diagnosis of HIV Infection	
Detection and Diagnosis of HBV Infection	
Detection and Diagnosis of HCV Infection	
RISK OF OCCUPATIONAL TRANSMISSION OF HIV FROM PATIENTS TO WORKERS	
Risk of HIV Infection Postexposure	
HIV Seroprevalence among Patients	
Incidence of Occupationally Acquired HIV Infection	
HIV Seroprevalence Surveys among HCWs	
RISK OF OCCUPATIONAL TRANSMISSION OF HBV FROM PATIENTS TO WORKERS	
Risk of HBV Infection Postexposure	
HBV Seroprevalence among Patients	
Trends in the Incidence of Occupationally Acquired HBV Infection	
HBV Prevalence among HCWs	
RISK OF OCCUPATIONAL TRANSMISSION OF HCV FROM PATIENTS TO WORKERS	
Risk of HCV Infection Postexposure	
HCV Seroprevalence among Patients	
HCV Seroprevalence among HCWs	
PREVENTION OF OCCUPATIONAL EXPOSURES TO BLOOD	
Standard Precautions	
Personal Protective Barriers, Work Techniques, and Safety Devices	
Sterilization, Disinfection, and Environmental Concerns	
VACCINATION AGAINST HBV INFECTION	
Prevention of HBV Infection Using Hepatitis B Vaccine	
Hepatitis B Vaccination Coverage among HCWs	
MANAGEMENT OF OCCUPATIONAL EXPOSURES	
Exposure Reporting	
Exposure Assessment and Emergency Management	
Postexposure Chemoprophylaxis for HIV	
Background	
Animal studies	
Human studies	
PHS recommendations for chemoprophylaxis	
Counseling and follow-up	
Toxicity	
Postexposure Prophylaxis for HBV	
Postexposure Management of HCV	
HCV prophylaxis	
Follow-up of HCWs after an occupational exposure to HCV	
MANAGEMENT OF INFECTED HCWS	
Transmission of HIV from Infected HCWs to Patients	
Retrospective investigation data	
Transmission of HBV from Infected HCWs to Patients	
Transmission of HCV from Infected HCWs to Patients	

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Prevention of Infection Transmission from Infected HCWs to Patients	401
Prevention of HIV and HBV transmission during invasive procedures	
HCWs with Blood-Borne Viruses	
CONCLUSION	
REFERENCES	

#### **INTRODUCTION**

Exposure to blood-borne pathogens poses a serious risk to health care workers (HCWs). Transmission of at least 20 different pathogens by needlestick and sharps injuries has been reported (79). Despite improved methods of preventing exposure, occupational exposures will continue to occur.

Assessment of the risk of blood-borne pathogen transmission in the health care setting requires information derived from various sources, including surveillance data, studies of the frequency and preventability of blood contacts, seroprevalence studies among patients and HCWs, and prospective studies that assess the risk of seroconversion after an exposure to infected blood. Factors influencing the risk to an individual HCW over a lifetime career include the number and types of blood contact experienced by the worker, the prevalence of blood-borne pathogen infection among patients treated by the worker, and the risk of transmission of infection after a single blood contact.

In this article, we review the risk and management of the three blood-borne viruses most commonly involved in occupational transmission: human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). We also will discuss current methods of preventing exposure, including standard precautions and the use of safety devices in the health care setting, as well as recommendations for postexposure prophylaxis.

# TRANSMISSION OF BLOOD-BORNE PATHOGENS IN THE HEALTH CARE SETTING

# Modes of Blood-Borne Pathogen Transmission

In the health care setting, blood-borne pathogen transmission occurs predominantly by percutaneous or mucosal exposure of workers to the blood or body fluids of infected patients. Occupational exposures that may result in HIV, HBV, or HCV transmission include needlestick and other sharps injuries; direct inoculation of virus into cutaneous scratches, skin lesions, abrasions, or burns; and inoculation of virus onto mucosal surfaces of the eyes, nose, or mouth through accidental splashes. HIV, HBV, and HCV do not spontaneously penetrate intact skin, and airborne transmission of these viruses does not occur.

#### **Epidemiology of Blood Contact**

To understand the nature, frequency, and prevention of percutaneous injuries and mucocutaneous blood contacts among HCWs, prospective observational studies have been performed in different patient care settings (Table 1). The percentage of procedures with at least one blood contact of any type ranged from 3% of procedures performed by invasive radiology personnel in a study in Dallas, Tex. (130), to 50% of procedures performed by surgeons in a study in Milwaukee, Wisc. (224). The percentage of procedures with at least one injury caused by a sharp instrument also varied widely, from 0.1 to 15%. These differences may be related to variations in study methods, procedures observed, and precautions used by the workers performing the procedures.

Several of these studies assessed specific risk factors for injury or exposure. For example, of the 99 percutaneous injuries observed by Tokars et al. during 1,382 operations in five different surgical specialties (general, orthopedic, gynecologic, trauma, and cardiac), most (73%) were related to suturing (256). Rates were highest (10%) during gynecologic surgeries (256). Panlilio et al. found in their study of blood contacts during surgery that risk factors for blood contacts by surgeons included performing an emergency procedure, patient blood loss greater than 250 ml, and surgery duration greater than 1 h

Specialty and authors (reference)	Yr	Location(s)	No. of procedures observed	No. of procedures with $\geq 1$ blood contact	% Procedures with ≥1 sharps injury
Surgery					
Tokars et al. (256)	1990	New York, N.Y.; Chicago, Ill.	1,382	46.6	6.9
Popejoy et al. (220)	1988	Albuquerque, N.Mex.	684	27.8	3.1
Quebbeman et al. (224)	1990	Milwaukee, Wisc.	234	50.4	15.4
Gerberding et al. (116)	1988	San Francisco, Calif.	1,307	6.4	1.3
Panlilio et al. (208)	1988–1989	Atlanta, Ga.	206	30.1	4.9
Obstetrics					
Panlilio et al. (210)	1989	Atlanta, Ga.	230	32.2	1.7
Invasive radiology					
Hansen et al. (130)	1992	Dallas, Tex.	501	3.0	0.6
Emergency room					
Marcus et al. (178)	1989	New York, N.Y.; Chicago, Ill.; Baltimore, Md.	9,793	3.9	0.1
Dentistry					
Cleveland et al. (77)	1993	New York, N.Y.	16,340	$NA^{a}$	0.1

TABLE 1. Prospective observational studies of blood contact among HCWs

<sup>a</sup> NA, not available.

	HBsAg	A	Anti	Anti-HBc		A
Stage of infection		Anti-HBs	Total <sup>b</sup>	IgM	HBeAg	Anti-HBe
Late incubation period	+	_	_	_	+ or –	_
Acute hepatitis B	+	_	+	+ + +	+	_
HBsAg carrier	+	-(+ rarely)	+	_	+ or -	+ or –
Recent (<6 months; resolved infection <sup>c</sup> )	_	++	++	+	-	+ or -
Distant (>6 months; resolved infection <sup><math>c</math></sup> )	_	++	++	_	-	+ or –
Vaccinated	_	++	_	_	_	_

TABLE 2. HBV serologic markers in different stages of infection and convalescence  $(201a)^a$ 

<sup>a</sup> +, positive; ++, strongly positive; +++, very strongly positive; + or -, variable reaction; -, negative.

<sup>b</sup> The total anti-HBc assay detects both IgM and IgG antibody.

<sup>c</sup> Resolved, the patient no longer has the disease.

(208). In their study of dental procedures, Cleveland et al. found that most percutaneous injuries sustained by dental residents occurred extraorally and were associated with denture impression procedures (77).

Retrospective studies and surveys have also shown high rates of blood contact among HCWs in different patient care settings. Tokars et al. found that among 3,420 participants at the American Academy of Orthopaedic Surgeons annual meeting, 87.4% of surgeons surveyed reported a blood-skin contact and 39.2% reported a percutaneous blood contact in the previous month (258). In a retrospective survey by O'Briain in 1991 (202), 56% of 36 resident and staff pathologists reported that they had sustained a cut or needlestick injury in the preceding year. In this study, pathologists reported 72 injuries, corresponding to a rate of one injury for every 37 autopsies performed and one injury for every 2,629 surgical specimens handled (202). An anonymous national survey of certified nurse-midwives by Willy et al. found that 74% had soiled their hands with blood, 51% had splashed blood or amniotic fluid in their faces, and 24% had sustained one or more needlestick injuries in the preceding 6 months (281). Among 550 medical students and residents in Los Angeles, Calif., who were surveyed anonymously by O'Neill et al., 71% reported exposures to patients' blood and body fluids during the preceding year (204). In a recent study of third- and fourth-year medical students in San Francisco, Calif., by Osborn et al., 12% reported an exposure to infectious body substances over the 7-year study period, from 1990 to 1996 (205). There is evidence among some groups of HCWs, such as dentists, that rates of exposure are decreasing over time, temporally associated with increased awareness and compliance with the practice of standard precautions (76).

# DETECTION AND DIAGNOSIS OF BLOOD-BORNE PATHOGEN INFECTIONS

An understanding of the detection and diagnosis of HIV, HBV, and HCV infection is vital for the appropriate management and care of HCWs exposed to or infected with bloodborne viruses.

#### **Detection and Diagnosis of HIV Infection**

After initial primary infection with HIV, there is a window period prior to the development of detectable antibody. In persons with known exposure dates, the estimated median time from initial infection to the development of detectable antibody is 2.4 months; 95% of individuals develop antibodies within 6 months of infection (34). Among HCWs with a doc-

umented seroconversion to HIV, 5% tested negative for HIV antibodies at >6 months after their occupational exposure but were seropositive within 12 months (73). The two antibody tests commonly used to detect HIV are the enzyme immunoassay (EIA) and the Western blot. An HIV test result is reported as negative when the EIA result is negative. The result is reported as positive when the EIA result is repeatedly reactive and when the result of a more specific, supplemental confirmatory test, such as the Western blot, is also positive. Once an individual develops an antibody response, it usually remains detectable for life. HIV infection for longer than 6 months without detectable antibody is uncommon (73, 226).

Direct virus assays (e.g., PCR for HIV RNA) are sensitive methods for the detection of HIV infection. However, problems with laboratory contamination, false-positive rates, and increased costs limit their routine use. While PCR for HIV RNA is approved for use in established HIV infection, its reliability in detecting very early infection has not been determined (34). At present, the false-positive and false-negative rates of PCR are too high to warrant a broader role for it in routine postexposure management (207).

#### **Detection and Diagnosis of HBV Infection**

The incubation period for acute hepatitis B ranges from 45 to 160 days, with an average of 120 days. Exposure to HBV can lead to an acute infection which may result in a chronic infection. Acute hepatitis B resembles other forms of viral hepatitis and cannot be distinguished based on history, physical examination, or serum biochemical tests.

The diagnosis of acute HBV infection is confirmed by the demonstration in serum of hepatitis B surface antigen (HBsAg), which appears well before onset of symptoms and before development of antibody to hepatitis B core antigen (anti-HBc), and immunoglobulin M (IgM) antibody to HBc, which appear at approximately the same time as symptoms (143). The presence of IgM anti-HBc indicates recent HBV infection, usually within the preceding 4 to 6 months. The presence of hepatitis B e antigen (HBeAg) in serum correlates with HBV replication, high titers of HBV, and infectivity. Persons who are positive for HBeAg typically have 10<sup>8</sup> to 10<sup>9</sup> HBV particles per ml of blood (243). In persons who resolve acute HBV infection, antibody to HBsAg (anti-HBs) develops and indicates immunity. The persistence of HBsAg for 6 months after the diagnosis of acute HBV is indicative of progression to chronic HBV infection.

HBV serologic markers in different stages of infection and convalescence are summarized in Table 2. Anti-HBc indicates prior infection and lasts indefinitely. In persons who

Test and type	Description	Application(s)	Comments
Anti-HCV	EIA and supplemental assay (i.e., recombinant immuno- blot assay [RIBA])	Indicates past or present infection but does not differentiate between acute, chronic, or resolved infection; all positive EIA results should be verified by a supplemental assay	Sensitivity ≥97%; EIA alone has low positive predictive value in low- prevalence populations
HCV RNA			
Qualitative tests <sup>b,c</sup>	Reverse transcriptase PCR (RT-PCR) amplification of HCV RNA by in-house or commercial assays (e.g., Amplicor HCV)	Detects presence of circulating HCV RNA; for monitoring patients on antiviral therapy	Detects virus as early as 1–2 weeks after exposure; detection of HCV RNA during course of infection may be intermittent (a single negative RT-PCR result is not conclusive); false-positive and false- negative results might occur
Quantitative tests <sup>b,c</sup>	RT-PCR amplification of HCV RNA by in-house or commercial assays (e.g., Amplicor HCV Monitor); branched-chain DNA assays (e.g., Quantiplex HCV RNA Assay)	Determines concentration of HCV RNA; may be useful for assessing the likelihood of response to antiviral therapy	Less sensitive than qualitative RT-PCR; should not be used to exclude the diagnosis of HCV infection or to determine treatment endpoint
Genotyping <sup>b,c</sup>	Several methodologies available (e.g., hybrid- ization, sequencing)	Groups isolates of HCV based on genetic differences into six genotypes and >90 subtypes; with new therapies, length of treatment may vary based on genotype	Genotype 1 (subtypes 1a and 1b) most common in United States and associated with lower response to antiviral therapy
Serotyping <sup>b</sup>	EIA based on immunoreactivity to synthetic peptides (e.g., Murex HCV Serotyping 1-6 Assay)	No clinical utility	Cannot distinguish between subtypes; dual infections often observed

TABLE 3. Tests for HCV infection<sup>a</sup>

<sup>a</sup> Adapted from reference 64a.

<sup>b</sup> Currently not FDA approved; lack standardization.

<sup>c</sup> Samples require special handling (e.g., serum must be separated within 2 to 4 h of collection and stored frozen [-20 or  $-70^{\circ}$ C]; samples should be shipped on dry ice).

respond to the hepatitis B vaccine, anti-HBs is the only antibody that is elicited. Persons with chronic infection who have mutations in the precore region of the HBV genome that prevent the expression of HBeAg but allow the expression of infectious virus have been described (40, 260). High titers of HBsAg can be observed in these persons even though they are HBeAg negative. The prevalence of these precore mutations in persons in the United States is unknown. The prevalence may be relatively high in certain parts of the world (41, 124, 171, 173, 197).

#### **Detection and Diagnosis of HCV Infection**

The incubation period for acute HCV infection ranges from 2 to 24 weeks, with an average of 6 to 7 weeks (166, 179; L. B. Seef, Letter, Ann. Intern. Med. 115:411, 1991). Because different types of viral hepatitis are indistinguishable based on clinical symptoms alone, serologic testing (Table 3) is necessary to establish a specific diagnosis of hepatitis C (121). Screening EIA and supplemental immunoblot assays are licensed and commercially available to detect antibodies to HCV (anti-HCV) (283). Because the rate of false positivity for the screening EIA is high in many populations, including HCWs, supplemental immunoblot assays must be used to judge the validity of repeatedly reactive EIA results. Anti-HCV may be detected within 5 to 6 weeks after the onset of infection and remains detectable long after the primary infection. In general, the interpretation of serologic tests for anti-HCV is limited by the following factors: (i) assays for anti-HCV do not distinguish between acute, chronic, or past infection; (ii) in acute infection there may be a prolonged interval between onset of illness

and anti-HCV seroconversion (though most infected individuals seroconvert within 3 months of exposure); and (iii) the detection of anti-HCV does not necessarily indicate active HCV replication (8).

HCV RNA can be detected in serum or plasma within 1 to 2 weeks of exposure to the virus and several weeks before onset of alanine aminotransferase (ALT) elevations or the appearance of anti-HCV (103). In patients with chronic HCV infection, HCV RNA levels may remain relatively stable or can fluctuate over 1,000,000-fold. Fluctuations in HCV RNA may or may not correlate with elevations in transaminase levels. Rarely, the detection of HCV RNA may be the only evidence of HCV infection (14).

PCR techniques to amplify reverse-transcribed cDNA are currently the most sensitive methods for detecting HCV RNA. Both qualitative (122) and quantitative (87, 229) methods can be used to detect HCV RNA. Quantitative assays are less sensitive than qualitative assays and should not be used as a primary test to confirm or exclude the diagnosis of HCV infection (212). Currently, testing for HCV RNA is available on a research basis and no tests have been approved by the U.S. Food and Drug Administration. Because of assay variability, results of HCV RNA testing should be interpreted cautiously.

There are at least six different genotypes and more than 90 subtypes of HCV (33). About 70% of HCV-infected persons in the United States are infected with genotype 1; subtype 1a predominates over subtype 1b. Several different nucleic acid detection methods are commercially available to group isolates of HCV based on genotypes and subtypes (172).

Authors (reference)	Yr	Setting	Location	No. of patients tested	No. of patients HIV positive (%)
Kelen et al. (158)	1987	Emergency department	Baltimore, Md.	2,302	119 (5.2)
Kelen et al. (157)	1988	Emergency department	Baltimore, Md.	2,544	152 (6.0)
Marcus et al. (178)	1989	Emergency department	Six high-AIDS areas	20,382	a
Nagachinta et al. (191)	1990	Emergency department	Los Angeles, Calif.	1,945	40 (2.1)
Mullins and Harrison (190)	1987-1991	Trauma center	Wichita, Kans.	2,004	3 (0.15)
Gordin et al. (119)	1987	Hospital	Washington, D.C.	616	23 (3.7)
Trepka et al. (261)	1993	Hospital	Denver, Colo.	2,825	155 (5.5)
Charache et al. (68)	1989	Elective surgery	Baltimore, Md.	4,087	18 (0.4)
Montecalvo et al. (187)	1992	Surgery-obstetrics	Valhalla, N.Y.	1,056	15 (1.4)
Krasinsi et al. <sup>b</sup>	1986-1987	Obstetrics	New York, N.Y.	1,192	28 (2.4)
Donegan et al. (94)	1987-1990	Obstetrics	Boston, Mass.	3,845	93 (2.4)

TABLE 4. HIV seroprevalence in emergency, hospital, surgery, and obstetrics patients

<sup>*a*</sup> 4.1 to 8.9 patients per 100 patient visits.

<sup>b</sup> K. Krasinski, W. Borkowsky, D. Bebenroth, and T. Moore, Letter, N. Engl. J. Med. 318:185, 1988.

# RISK OF OCCUPATIONAL TRANSMISSION OF HIV FROM PATIENTS TO WORKERS

# **Risk of HIV Infection Postexposure**

Prospective studies of HCWs have estimated that the average risk for HIV transmission after a percutaneous exposure to HIV-infected blood is approximately 0.3% (95% confidence interval = 0.2 to 0.5%) (23) and that after a mucous membrane exposure it is 0.09% (95% confidence interval = 0.006 to (0.5%) (147). The risk after a cutaneous exposure is less but has not been well quantified since no HCW enrolled in a prospective study has seroconverted after an isolated skin exposure. There are insufficient data to quantify the risk of transmission after occupational exposure to potentially infectious tissues or fluids other than blood. However, in a study by Fahey et al., none of 559 participants reporting cutaneous exposures to blood, sputum, urine, feces, or other body substances from patients presumed infected with HIV acquired HIV infection (102). There is also no evidence of a risk for HIV transmission by the aerosol route. Transmission of HIV by aerosol would require the generation of aerosolized particles of blood, the presence of infective HIV in these aerosolized particles, and the deposition of a sufficient number of infective particles in the respiratory tract or on the mucous membranes of a susceptible host to cause infection. Biological or epidemiologic evidence that HIV can be transmitted by aerosols via the respiratory route currently does not exist (22). Although not specifically designed to assess the possibility of aerosol transmission of HIV, the 1991 seroprevalence survey of attendees of the annual meeting of the American Academy of Orthopaedic Surgeons addressed this concern indirectly (258). There were 1,201 study participants without nonoccupational risk factors who had participated in procedures on patients with HIV infection or AIDS and had never used a "space suit" or other device to prevent inhalation of aerosols. Since power instruments are used frequently in orthopedic procedures, many of these participants may have been exposed to blood or tissue aerosols produced by these instruments; all were HIV seronegative (258).

The risk of HIV transmission after a percutaneous exposure appears to be influenced by several factors. To assess possible risk factors, the Centers for Disease Control and Prevention (CDC), in collaboration with international public health authorities, conducted a retrospective case-control study using data reported to national surveillance systems in the United States, France, Italy, and the United Kingdom. Based on logistic regression analysis, factors associated with HIV transmission after percutaneous exposure included a deep injury, a device visibly contaminated with the source patient's blood, procedures involving a needle placed directly in the patient's vein or artery, and a source patient who died from AIDS within 60 days of the exposure (39). The findings of the case-control study suggest that the risk for HIV infection likely exceeds 0.3% for percutaneous injuries involving a larger volume of blood and/or higher titer of HIV in the blood. Several laboratory studies support these findings. In vitro models have shown that increasing needle size and penetration depth are associated with increased blood transfer volume (182), that hollowbore needles transfer greater volumes of blood than solid suture needles, and that gloves reduce the amount of blood transferred (26). Studies also have shown that the level of infectious  $\dot{HIV}$  present in the blood of most patients with symptomatic AIDS is significantly higher than the level present in patients with asymptomatic HIV infection (141). An additional finding of the case-control study was that postexposure use of zidovudine (ZDV) by HCWs was associated with a lower risk for HIV transmission (39). (This issue will be discussed in more detail in the section Postexposure Chemoprophylaxis for HIV [below]). It is also possible that host defense mechanisms influence the risk of HIV transmission. One study demonstrated an HIV-specific T-helper cellular immune response when peripheral blood mononuclear cells from a small number of HCWs exposed to HIV were stimulated in vitro by HIV. None of the HCWs seroconverted. One possible explanation for these observations is that host immune responses prevented establishment of HIV infection after exposure (75). Similar cytotoxic T-lymphocyte responses have been observed in other populations with repeated HIV exposure without resulting infection (70, 74, 160, 170, 225).

#### **HIV Seroprevalence among Patients**

In the United States, HIV seroprevalence rates vary widely by geographic area and patients' demographic characteristics. The CDC's Sentinel Hospital Surveillance System tested 195,829 anonymous patient blood samples at 20 hospitals in 15 cities between September 1989 and October 1991. The HIV seroprevalence at these institutions ranged from 0.2 to 14.2% and was highest among men aged 25 to 44 years and patients with infectious conditions (excluding symptomatic HIV infection) and drug-related conditions (153).

Similarly, seroprevalence data for unselected hospital admissions and for patients presenting to emergency departments, operating rooms, and obstetrical units have demonstrated considerable variation (Table 4). The lowest seroprevalence rates

 TABLE 5. HCWs with documented and possible occupationally acquired HIV infection reported through June 1999 in the United States<sup>a</sup>

Occupation	No. of documented cases of occupational transmission	No. of possible cases of occupational transmission
Dental worker, including dentist		6
Embalmer or morgue technician	1	2
Emergency medical technician		12
or paramedic		
Health aide or attendant	1	15
Housekeeper or maintenance worker	1	12
Laboratory technician, clinical	16	16
Laboratory technician, nonclinical	3	
Nurse	23	34
Physician, nonsurgical	23 6	54 12
Physician, surgical	0	6
Respiratory therapist	1	2
Technician, dialysis	1	3
Technician, surgical	2	2
Technician or therapist, other	2	10
Other health care occupations		4
Total	55	136

<sup>*a*</sup> HCWs are defined as those persons, including students and trainees, who have worked in a health care, clinical, or HIV laboratory setting at any time since 1978. Adapted from reference 65.

have been reported in rural and suburban areas: 0.15% among trauma patients in Wichita, Kans. (190), and 0.4% among elective surgery patients in suburban Baltimore, Md. (68). The highest seroprevalence rates have been reported in urban, inner-city populations: 5.2 to 6.0% among emergency department patients in inner-city Baltimore, Md. (157, 191), and 5.5% among non-obstetric hospitalized patients in Denver, Colo. (K. Krasinski, W. Borkowski, D. Bebenroth, and T. Moore, Letter, N. Engl. J. Med. **318**:185, 1988).

In a CDC study conducted in six emergency departments in three urban and three suburban areas of New York, N.Y., Chicago, Ill., and Baltimore, Md., the overall rate of HIV infection ranged from about 4 to 9 per 100 patient visits (178). The study found that many patients' HIV infections were unrecognized at the time of initial presentation to the hospital. The percentage of patients whose HIV infection was unknown to hospital emergency department workers was about 70% in the three inner city hospitals and ranged from 40 to 90% in the three suburban hospitals.

# **Incidence of Occupationally Acquired HIV Infection**

As of 30 June 1999, a total of 191 U.S. workers had been reported to the CDC's national surveillance system for occupationally acquired HIV infection (Table 5) (65). Fifty-five HCWs had known occupational HIV exposures, with a base-line negative HIV test and subsequent documented seroconversion. Fifty of these exposures were to HIV-infected blood, one was to visibly bloody fluid, one was to an unspecified fluid, and three were to concentrated virus in a laboratory. Of the 55 HCWs, 47 sustained percutaneous exposures, 5 had mucocutaneous exposure, 2 had both a percutaneous and a mucocutaneous exposure, and 1 had an unknown route of exposure. Twenty-five of these HCWs have developed AIDS.

Of the 191 U.S. workers reported to the CDC's surveillance system, 136 have been reported as possible cases of occupa-

tionally acquired HIV infection. None of these HCWs reported behavioral or blood transfusion risk factors, and all reported occupational exposures to blood, body fluids, or laboratory specimens containing HIV. However, the time or source of infection was undocumented, usually because no baseline serum sample was available to establish seronegativity at the time of exposure.

The CDC's surveillance system likely does not reflect the full extent of occupationally acquired HIV infection because of underreporting of known infections or underrecognition of HIV infection. Studies of HCWs in hospital settings suggest that many percutaneous injuries are not reported (129, 177). Also, HCWs may not complete postexposure follow-up serologic testing (D. Cardo and the Health Care Worker Surveillance Study Group, Abstr. 6th Annu. Meet. Soc. Healthcare Epidemiol. Am., abstr. 67, 1996).

#### HIV Seroprevalence Surveys among HCWs

HIV seroprevalence surveys provide a way of indirectly assessing the risk of occupationally acquired HIV infection. The CDC has conducted two voluntary anonymous seroprevalence surveys of surgeons in different specialties. In 1992, a seroprevalence survey was done among general surgeons, obstetricians, gynecologists, and orthopedic surgeons practicing in moderate to high AIDS incidence areas. Of the 770 participating surgeons, one general surgeon, who reported nonoccupa-

TABLE 6. Published HIV seroprevalence in selected HCWs

Occupation and authors (reference)	No. of HCWs tested	No. of HCWs HIV positive	% Prevalence
Surgeon			
Panlilio et al. (209)	770	1	0.13
Tokars et al. (258)	3,420	2	0
HCW blood donor			
Chamberland et al. (66)	9,449	3	a
U.S. Army Reserve physician, dentist			
Cowan et al. (82)	3,347	3	Not known
Dentist			
Flynn et al. (107)	89	0	0
Klein et al. $(163)$	$1,132^{b}$	1	0.09
Siew et al. <sup>c</sup>	1,195	0	0
Gruninger et al. (123)	1,165	1	0.09
Gruninger et al. (123)	1,433 <sup>b</sup>	0	0
Gruninger et al. (123)	$1,429^{b}$	Õ	Õ
Ebbesen et al. <sup><math>d</math></sup>	961	0	0
Hemodialysis staff			
Assogba et al. (20)	40	0	0
Chirgwin et al. (71)	25	0	Ő
Comodo et al. (80)	84	Ő	Ő
Goldman et al. (118)	49	0	0
Peterman et al. (215)	161	2	1.2
Mortician, embalmer			
Gershon et al. (117)	130	1	0.8
Turner et al. (264)	$130^{1}$	0	0.8
1 uinei et al. (204)	129	U	0

<sup>a</sup> One HCW lost to follow-up.

<sup>b</sup> Persons with nonoccupational risk excluded.

<sup>c</sup> C. Siew, S. E. Gruninger, and S. A. Hojvat, Letter, N. Engl. J. Med. 318:1400–1401, 1988.

<sup>d</sup> P. Ebbesen, M. Melbye, F. Scheutz, A. J. Bodner, and R. J. Bigger, Letter, JAMA 256:2199, 1986.

tional risk factors for HIV infection on an anonymous questionnaire, was HIV positive (209). In 1991, a seroprevalence survey was done among surgeons attending the annual meeting of the American Academy of Orthopaedic Surgeons. Of the 3,420 participants, two surgeons, both of whom reported nonoccupational risk factors, were HIV positive (258). Other seroprevalence studies similarly have shown low rates of HIV seropositivity among HCWs without nonoccupational risk factors for HIV infection (Table 6) (20, 66, 71, 80, 82, 107, 117, 118, 123, 163, 215, 264; P. Ebbensen, M. Melbye, F. Scheutz, A. J. Bodner, and R. J. Bigger, Letter, JAMA **256**:2199, 1986; C. Siew, S. E. Gruninger, and S. A. Hojvat, Letter, N. Engl. J. Med. **318**:1400–1401, 1988).

One limitation of seroprevalence studies is that the extent of occupational and nonoccupational exposure to HIV among tested workers is usually unknown. Also, the rates may be underestimates if individuals deferred testing because they knew they were or suspected they might be HIV positive. Nonetheless, these seroprevalence surveys indicate that there was not a high rate of undetected HIV infection among the HCWs studied, many of whom had substantial opportunity for occupational exposures.

# RISK OF OCCUPATIONAL TRANSMISSION OF HBV FROM PATIENTS TO WORKERS

#### **Risk of HBV Infection Postexposure**

The probability of HBV transmission after an occupational exposure is dependent upon the concentration of infectious virions in the implicated body fluid, the volume of infective material transferred, and the route of inoculation (e.g., percutaneous or mucosal).

HBV is present in high titers in blood and serous fluids, ranging from a few virions to  $10^9$  virions per ml (142). The virus is present in moderate titers in saliva, semen, and vaginal secretions (154). The titer in semen and saliva is generally 1,000 to 10,000 times lower than the corresponding titer in serum (44, 269). Other body fluids such as urine and feces contain very low levels of HBV unless contaminated with blood (91, 106, 149).

One of the most common modes of HBV transmission in the health care setting is an unintentional injury of an HCW from a needle contaminated with HBsAg-positive blood from an infected patient (5). The average volume of blood inoculated during a needlestick injury with a 22-gauge needle is approximately 1 µl (V. M. Napoli and J. E. McGowan, Letter, J. Infect. Dis. 155:828, 1987), a quantity sufficient to contain up to 100 infectious doses of HBV (243). The risk of transmission after a needlestick exposure to a nonimmune person is at least 30% if the source patient is HBeAg positive but is less than 6% if the patient is HBeAg negative (17, 120, 277). Blood from patients with HBsAg titers below the threshold of detection using routine serologic tests is rarely infectious (4). While overt percutaneous injuries are efficient modes of HBV transmission, other less-obvious exposures may also lead to occupationally acquired HBV infection. In a case series of HBV-infected HCWs, fewer than 10% recalled a specific percutaneous injury, while 29 to 38% recalled caring for an HBsAg-positive patient within 6 months prior to their onset of illness (35; A. K. R. Chaudhuri and E. A. C. Follet, Letter, Br. Med. J. 284:1408, 1982).

#### **HBV** Seroprevalence among Patients

The risk of acquiring HBV is related to the prevalence of HBV infection in the patient population with which the HCW

works. Patients who are HBsAg positive, either from acute or chronic infection, are potential sources of infection. Patients who are acutely infected may not be recognized since acute infection is symptomatic in only 10% of children and 30 to 50% of adults. Chronic HBV infection is often asymptomatic. HCWs who work in settings with patient populations with a relatively high prevalence of HBV infection, such as urban and tertiary-care hospitals (which more commonly serve groups at high risk for HBV infection, such as injecting drug users), have been shown to be at greater risk of occupational HBV infection than those who work in rural or community hospitals (133).

Prior to the implementation of guidelines for hepatitis B prevention, patients in hemodialysis centers had high rates of HBV infection, which posed an increased risk for workers in this setting (43, 189). However, between 1976 and 1993, the annual incidence of HBV infection decreased from 3.0 to 0.1% among hemodialysis patients and from 2.6 to 0.02% among staff members (254). Outbreaks of HBV infection in hemodialysis centers rarely occur today. When these outbreaks do occur, they are most often traced to failure to implement recommended infection control practices (11, 56, 198).

#### Trends in the Incidence of Occupationally Acquired HBV Infection

The number of HCWs infected annually with HBV in the United States is estimated from data reported to the CDC Viral Hepatitis Surveillance Program (VHSP). Annual estimates are derived by applying the proportion of people who acquired HBV occupationally in the health care setting in a given year as reported to the VHSP to the estimated number of HBV infections that occurred in that same year. For example, the CDC estimates that in 1985 about 12,000 HCWs became infected with HBV (48). This figure is derived from the proportion of people who acquired HBV occupationally in the health care setting in 1985 (6% of patients in the Viral Hepatitis Surveillance Program reported employment in a medical or dental field for 6 months prior to date onset of illness, and two-thirds of these patients were estimated to work in settings with potential exposure to blood or body fluids) and the estimated number of HBV infections that occurred in the United States in 1985 (300,000).

The incidence of HBV infection among HCWs has decreased substantially since the early 1980s (54). The estimated number of HBV infections among HCWs declined from 17,000 (386 per 100,000) in 1983 to 400 (9.1 per 100,000) in 1995 (176). The estimated incidence of HBV infections among HCWs in 1983 was about threefold higher than the incidence of HBV infections in the general U.S. population (122 per 100,000) and declined by 1995 to more than fivefold lower than the incidence in the general U.S. population (50 per 100,000).

The absolute decline in the number of HBV infections among HCWs is attributed to the implementation of standard precautions in health care settings, including the increasing use of barrier precautions and personal protective devices and increasing levels of hepatitis B vaccination coverage among HCWs (21, 126, 282) (see Hepatitis B Vaccination Coverage among HCWs [below]).

#### **HBV Prevalence among HCWs**

Prior to the availability of the hepatitis B vaccine, numerous cross-sectional surveys showed that HCWs had a three- to fivefold higher seroprevalence of HBV infection than the general U.S. population (48, 89, 93, 239, 241, 253). Prevalence rates of HBV infection of 13 to 18% have been demonstrated

among surgeons, and infection rates up to 27% have been demonstrated among dentists and oral surgeons (246, 278). By comparison, about 4% of first-time blood donors in the United States during the 1970s had serological markers of HBV infection (246).

Prevalence of previous infection with HBV has been found to increase with increasing age and to be directly related to the number of years employed as an HCW (78, 209, 241, 253). HCWs with frequent blood or needlestick exposures have a twofold higher prevalence of HBV infection than other HCWs (125). Physicians and dentists in specialties that involve frequent blood or needlestick exposure (e.g., obstetrician-gynecologists, pathologists, and oral surgeons) have a significantly elevated risk of HBV infection compared to specialists with less-frequent blood or needlestick exposure (e.g., pediatricians and psychiatrists) (278).

# RISK OF OCCUPATIONAL TRANSMISSION OF HCV FROM PATIENTS TO WORKERS

#### **Risk of HCV Infection Postexposure**

HCV is transmitted efficiently by large exposures to blood such as through transfusion of blood or blood products from infectious donors. Overt percutaneous exposures to HCV (e.g., accidental needlestick injuries) also have been documented as means of HCV transmission.

The risk that an HCV-infected individual will transmit the virus may be related to the type and size of the inoculum and the route of transmission as well as the titer of virus, but data on the threshold concentration of virus needed to transmit infection are insufficient. Neither the presence of antibody nor the presence of HCV RNA is a direct measure of infectivity.

Prior to the discovery of HCV, a significant association was noted between acquiring acute non-A, non-B (NANB) hepatitis and employment in patient care and laboratory work (12). A case-control study among British blood donors found that having been an HCW was a risk factor for having HCV infection (196). A number of case reports have documented occupational HCV transmission from anti-HCV-positive patients to HCWs in a variety of settings (234, 263, 268; A. M. Herbert, D. M. Walker, K. L. Davies, and J. Bagg, Letter, Lancet 339: 305, 1992; A. B. Jochen, Letter, Lancet 339:304, 1992; F. Marranconi, V. Mecenero, G. P. Pellizer, M. C. Bettini, M. Conforto, A. Vaglia, C. Stecca, E. Cardone, and F. de Lalla, Letter, Infection 20:111, 1992; E. Perez-Trallero, G. Cilla, and J. R. Saenz, Letter, Lancet 344:548, 1994). A history of accidental needlestick exposures among HCWs has also been independently associated with anti-HCV positivity (219).

Follow-up studies of HCWs who sustained percutaneous exposures to blood from anti-HCV-positive patients have found variable rates of HCV transmission (30, 140, 161, 223, 247, 284). However, the average incidence of anti-HCV seroconversion after needlestick or sharps exposure from a known anti-HCV-positive source patient is 1.8% (range, 0 to 7%) (10, 64). In one study conducted in Japan, which included PCR testing for HCV RNA in source patients and HCWs, the risk of transmission after a needlestick exposure from a source patient with HCV RNA-positive blood was 10% (186). No infections have been associated with mucous membrane or nonintact skin exposures in prospective studies conducted to date; however, there have been two case reports of HCV transmission as a result of a blood splash to the conjunctiva (232; G. Ippolito, V. Puro, N. Petrosillo, G. De Carli, G. Micheloni, and E. Magliano, Letter, JAMA 280:28, 1998).

The importance of mucous membrane and inapparent par-

enteral exposures in HCV transmission in the health care setting is not well defined. HCV typically circulates at low titers in infected serum in comparison to HBV (32, 88). Saliva may contain HCV but has not been epidemiologically linked to transmission. HCV RNA has not been detected in urine, feces, or vaginal secretions from patients who have virus circulating in the blood (96, 144). The relatively few studies examining risk factors for infection and conflicting results highlight the need for further studies to better define the factors influencing infectivity and risk factors for acquiring HCV infection among HCWs.

#### **HCV Seroprevalence among Patients**

The prevalence of anti-HCV among different population subgroups who may serve as a reservoir for transmission in the health care setting is highly variable in the United States (6). Anti-HCV seroprevalence rates among blood donors are <0.5%, while higher rates have been observed among hemodialysis patients ( $\sim 20\%$ ) and hemophilia patients ( $\sim 60\%$  to 90%) (15). The anti-HCV seroprevalence rates among hospitalized patients have been reported to range from 2 to 18% (159, 175). Data from the Third National Health and Examination Survey, conducted during the period 1988 to 1994, have indicated that an estimated 1.8% of Americans have been infected with HCV (13).

The prevalence of anti-HCV among persons on dialysis is consistently higher than in other hospitalized patient groups. The prevalence of anti-HCV among dialysis patients ranges from 8 to 36% in the United States (213) and from 1 to 47% worldwide (188). The increased prevalence of anti-HCV among patients on dialysis has been associated with several factors, including previous blood transfusion, increased years the patient has been on dialysis, mode of dialysis (patients on peritoneal dialysis are at lower risk than hemodialyzed patients), increased prevalence of HCV infection among patients in the dialysis unit, history of previous organ transplantation, and history of illegal injection drug use (194, 213). Studies have consistently demonstrated an association between anti-HCV positivity and increasing years on dialysis; this association is independent of blood transfusion (67, 110, 131, 134, 203, 240; U. Schlipkoter, M. Roggendorf, K. Cholmakov, A. Weise, V. Gladziwa, and N. Luz, Letter, Lancet 335:1409, 1990; K. Yamaguchi, Y. Nishimura, N. Fukoka, J. Machida, S. Veda, Y. Kusumoto, G. Futami, T. Ishii, and K. Takatsuki, Letter, Lancet 335:1409-1410, 1990).

#### **HCV Seroprevalence among HCWs**

Despite an increased HCV infection rate among dialysis patients, staff members of hemodialysis centers in the United States have been found to have prevalence rates similar to those seen in other HCWs (255). In general, seroprevalence surveys among hospital-based HCWs in western countries have found rates of anti-HCV similar to or lower than that estimated to occur in the general population (9, 195, 276; G. McQuillan, M. Alter, L. Moyer, S. Lambert, and H. Margolis, Proc. IX Int. Symp. Viral Hepatitis Liver Dis., p. 8, 1996). Even among HCWs with high rates of exposure to blood or needlestick injuries, seroprevalence rates similar to those found among blood donors (<0.5%) have been observed (249, 284).

The CDC determines national risk factor estimates for acute HCV infection through a program of intensive surveillance conducted in several sentinel counties. Between 1991 and 1998, approximately 4% of acute hepatitis C cases reported to this sentinel surveillance system were occupationally related (I. T. Williams, M. Fleenor, F. Judson, K. Mottram, H. Homan,

P. Ryder, and M. J. Alter, Abstr. 10th Int. Symp. Viral Hepatitis Liver Dis, p. 63, 2000).

Several studies examining risk factors for HCV infection among HCWs have produced conflicting results. One study in New York found 2% of dentists and 9% of oral surgeons to be anti-HCV positive (162). In that study, the percentage of professional time spent practicing oral surgery was directly related to anti-HCV positivity. However, anti-HCV-positive dentists reported 50% fewer needlesticks during the previous 5 years than did anti-HCV-negative dentists. In contrast, anti-HCV positivity was associated with a reported history of frequent needlestick injuries in a survey of hospital-based HCWs in California (219). However, in studies among surgeons in several urban areas, no association was observed with recollection of skin, mucous membrane, or percutaneous exposure to blood during the last month or year (209; J. I. Tokars, M. Chamberland, C. Shapiro, C. Schable, A. Wright, D. Culver, M. Jones, P. McKibben, D. Bell, and the Serosurvey Study Committee, Proc. 2nd Annu. Meet. Soc. Hosp. Epidemiol. Am., p. 33, 1992).

# PREVENTION OF OCCUPATIONAL EXPOSURES TO BLOOD

# **Standard Precautions**

In 1987 the CDC developed universal precautions to help protect both HCWs and patients from infection with bloodborne pathogens in the health care setting (46). These recommendations stress that blood is the most important source of HIV, HBV, and other blood-borne pathogens and that infection control efforts should focus on the prevention of exposures to blood as well as the receipt of HBV immunizations. In 1995, the CDC's Hospital Infection Control Practices Advisory Committee (HICPAC) introduced the concept of standard precautions, which synthesizes the major features of universal precautions and body substance isolation into a single set of precautions to be used for the care of all patients in hospitals regardless of their presumed infection status (111). Blood, certain other body fluids (e.g., semen, vaginal secretions, and amniotic, cerebrospinal, pericardial, peritoneal, and synovial fluids), and tissues of all patients should be considered potentially infectious (46, 47). Standard precautions apply to blood; all body fluids, secretions, and excretions (except sweat); nonintact skin; and mucous membranes (111). The core elements of standard precautions comprise (i) hand washing after patient contact, (ii) the use of barrier precautions (e.g., gloves, gowns, and facial protection) to prevent mucocutaneous contact, and (iii) minimal manual manipulation of sharp instruments and devices and disposal of these items in punctureresistant containers (46, 47, 111).

The CDC's recommendations—along with the blood-borne pathogen standard issued by the Occupational Safety and Health Administration (OSHA), which requires that HBV vaccine be made available to HCWs with risk of occupational exposure, the development of written exposure control plans, the use of engineering and work practice controls to reduce exposures, and annual HCW training (266)—have caused widespread adoption of standard precautions in U.S. hospitals. Several investigators have attempted to assess the efficacy of standard precautions. For example, Beekman et al. at the Clinical Center of the National Institutes of Health found a significant and sustained decrease in percutaneous injuries associated with the implementation of standard precautions (21). At the same institution, a comparison of the frequencies of HCWs' blood exposures on self-reported questionnaires before and after standard precaution training found a decrease in the mean number of blood exposures per year among clinical HCWs, from 35.8 to 18.1 (102). Education of HCWs about needlestick prevention, along with effective communication and convenient placement of sharps containers, has been shown to decrease needlestick injuries by 60% among HCWs at a teaching hospital in California (126).

# Personal Protective Barriers, Work Techniques, and Safety Devices

Skin and mucous membrane contacts frequently can be prevented with the use of barrier precautions, such as gloves, masks, gowns, and goggles, among HCWs in emergency room, operating room, and medical ward settings (102, 178, 259, 282). However, the greatest risk of blood-borne pathogen transmission comes from percutaneous injuries, which are not prevented by barriers but instead require changes in technique and/or use of safety devices. For instance, Tokars et al. noted that half of the percutaneous injuries during surgical procedures occurred when fingers, rather than instruments, were used during suturing, suggesting that the use of instruments or other changes in technique might reduce injuries (256). The use of blunt-tip suture needles during surgical procedures can significantly reduce suture-related percutaneous injuries. In a CDC study of blunt suture needle use during gynecological surgical procedures, researchers found no percutaneous injuries with blunt suture needles compared to 1.9 injuries per 1,000 conventional curved suture needles used and 14.2 injuries per 1,000 straight suture needles used (58).

Similarly, changes in the design of sharp instruments can prevent injuries in nonsurgical settings (151, 152). One study found that resheathable and bluntable needles reduced percutaneous injuries during phlebotomy by 23 to 76% (59). Many injuries in the health care setting are associated with intravenous (i.v.) tubing-needle assemblies. Studies have found that i.v.-related percutaneous injuries decreased approximately 72 to 100% following the introduction of needleless systems (112, 252; Skolnick et al., Letter, N. Engl. J. Med. 318:1400-1401); the greatest reductions were seen with those systems that did not permit needles to access i.v. lines. Although devices may be safer for HCWs, it is important that they be assessed for potential patient care complications. An outbreak of bloodstream infections associated with a needleless i.v. infusion system raised concerns regarding the potential for adverse patient outcomes associated with these devices (86). However, Adams et al. prospectively compared the incidences of various patientrelated adverse outcomes for conventional and needleless i.v. access systems and found that the needleless system posed no greater risk of positive catheter tip or adapter fluid cultures, i.v. site complications, or nosocomial bacteremia (1).

#### Sterilization, Disinfection, and Environmental Concerns

Most laboratory studies have indicated that HIV is readily susceptible to a variety of disinfectants (233). The titer of HIV is reduced by 90 to 99% within several hours after drying and then further diminishes with time (46, 267). The length of time that viable HIV can be detected depends on the conditions of the experiment, including the initial concentration of HIV, whether organic or other foreign material is present that may protect HIV from inactivation, and other factors. There is no evidence for HIV transmission by environmental surfaces.

In contrast, HBV is resistant to drying, ambient temperatures, simple detergents, and alcohol and has been found to be stable on environmental surfaces for at least 7 days (104, 211). Thus, indirect inoculation can occur via inanimate objects (e.g., contaminated medical equipment or environmental surfaces). However, HBV has been shown to be inactivated by several intermediate-level disinfectants, including 0.1% glutaraldehyde and 500-ppm free chlorine from sodium hypochlorite (i.e., household bleach) (29, 105). Heating to 98°C for 2 min also inactivates HBV (165).

While specific animal infectivity studies have not been published, rapid degradation of HCV occurs when serum containing HCV is left at room temperature (83). Epidemiologic data also suggest that environmental contamination with HCV is not a significant route of transmission in the health care setting.

Standard sterilization and disinfection procedures recommended for patient care equipment are adequate to sterilize or disinfect items contaminated with blood or other body fluids from people infected with blood-borne pathogens, including HIV, HBV, and HCV. Because foreign material may interfere with the sterilization or disinfection procedure, devices must first be adequately cleaned. Cleaning before disinfection is particularly important for devices such as endoscopes that may become heavily soiled and cannot tolerate heat sterilization (180).

All spills of blood and blood-contaminated body fluids should be promptly cleaned by a person wearing gloves and using an Environmental Protection Agency-approved disinfectant or a 1:10 to 1:100 solution of household bleach. Visible material should first be removed with disposable towels or other means to prevent direct contact with blood. The area should then be decontaminated with an appropriate disinfectant (46).

#### VACCINATION AGAINST HBV INFECTION

#### Prevention of HBV Infection Using Hepatitis B Vaccine

Hepatitis B vaccine provides both preexposure and postexposure protection against HBV infection. Two types of hepatitis B vaccine, plasma-derived and recombinant, have been licensed in the United States, and both are very effective in preventing HBV infection. The plasma-derived vaccine is no longer available in the United States. The currently available vaccines are produced by recombinant DNA technology (51). Three intramuscular doses of hepatitis B vaccine induce a protective antibody response in >90% of healthy recipients. Adults who develop a protective antibody response are protected from clinical disease and chronic infection. Long-term studies of immunized adults and children indicate that immune memory remains intact for at least 12 years, even though anti-HBs levels may become low or undetectable (272, 279, 280). Routine booster doses of hepatitis B vaccine are not considered necessary (61).

Since it became available in 1981, hepatitis B vaccine has been recommended for HCWs who have anticipated exposure to blood or body fluids. It is preferable that HCWs be vaccinated during professional training or early in their careers, so that they are protected prior to being at risk of occupational HBV infection.

Persons at occupational risk of infection should be tested for anti-HBs after vaccination, since knowledge of a person's HBV immune status allows for the most precise selection of a postexposure prophylaxis regimen, should an exposure occur. It is recommended that postvaccination testing be done for all HCWs who are at risk for having blood or blood-contaminated body fluid exposures (e.g., physicians, nurses, operating room technicians, dentists, dental hygienists, emergency medical technicians, phlebotomists, laboratory technologists and technicians, physician assistants, and nurse practitioners). Testing is not indicated for persons at low risk of mucosal or percutaneous exposure to blood or body fluids or HBV infection (e.g., public safety workers and HCWs without direct patient contact). When indicated, postvaccination testing should be done 1 to 2 months after completion of the three-dose series.

Persons who do not respond to the primary vaccine series should complete a second three-dose vaccine series or be evaluated to determine if they are HBsAg positive. Revaccinated persons should be retested at the completion of the second vaccine series. Nonresponders to vaccination who are HBsAg negative should be considered susceptible to HBV infection and should be counseled regarding precautions to prevent HBV infection and the need to obtain hepatitis B immunoglobulin (IG) prophylaxis for any known or probable parenteral exposure to HBsAg-positive blood.

#### Hepatitis B Vaccination Coverage among HCWs

Since 1982, hepatitis B vaccine has been recommended for HCWs with frequent blood or needle exposures (45). However, hepatitis B vaccine was not widely used among HCWs in the 1980s. In a survey of U.S. hospitals conducted during 1990 by OSHA, 91% of hospitals had hepatitis B vaccination programs for employees, and of these, 64% paid for the cost of vaccinating high-risk employees (i.e., those involved in direct patient care and laboratory work) (181). However, it was estimated that only 46% of high-risk employees had received the hepatitis B vaccine. Barriers to vaccine use among HCWs included the high cost of the vaccine, failure of employers to offer the vaccine at low or no cost, and a perception among some HCWs that they would not benefit from vaccination.

In 1991, OSHA issued a standard that required employers to offer hepatitis B vaccine at no cost to employees with reasonably anticipated contact with blood or other potentially infectious materials (266). This standard does not require the employer to conduct postvaccination testing or to provide booster doses of hepatitis B vaccine. Employees who administer first aid only as a collateral duty to their routine work assignment (e.g., teachers) do not need to be offered the hepatitis B vaccine until they give aid involving exposure to blood or other potentially infectious materials. If an exposure incident occurs, the employee should be evaluated for postexposure prophylaxis (PEP) in accordance with the recommendations of the Advisory Committee on Immunization Practices (ACIP) (60).

Subsequent to the issuance of the OSHA guidelines, hepatitis B vaccination coverage substantially increased among HCWs, especially among younger HCWs. In 1991 and 1992, surveys indicated that approximately 90% of orthopedic and hospital-based surgeons aged 20 to 29 years from urban areas had received the hepatitis B vaccine. However, among surgeons who had practiced more than 10 years, 25% had not received the hepatitis B vaccine and were susceptible to HBV infection (209; Tokars et al., Proc. 2nd Annu. Meet. Soc. Hosp. Epidemiol. Am., p. 33, 1992). A survey conducted among 150 hospitals in 1992 found that 51% of the employees who were eligible to receive hepatitis B vaccine had completed the vaccination series (2). By 1994, a telephone survey of 113 hospitals found that 67% of eligible employees had completed the hepatitis B vaccination series (176). Vaccination coverage was highest among personnel with frequent exposure to infectious body fluids and lowest for employees at low risk for exposure. Coverage levels among eligible employee groups surveyed in 1994 were 81% among phlebotomists, 72% among nurses, 71% among physicians and residents, 63% among nurse aides, 59%

among custodial and security personnel, 44% among clerical administrative staff, and 44% among food service workers.

#### MANAGEMENT OF OCCUPATIONAL EXPOSURES

Although exposure prevention remains the best strategy for protecting HCWs from occupationally acquired infection, exposures are nevertheless likely to occur. Employers should have in place a system that includes written protocols for prompt reporting, evaluation, counseling, treatment, and follow-up of occupational exposures that may place a worker at risk of blood-borne pathogen infection. Employers also must establish exposure control plans and comply with incident reporting requirements mandated by OSHA (50, 266). Access to clinicians who can provide postexposure care should be available during all work hours, including nights and weekends. Persons responsible for providing postexposure counseling should be familiar with evaluation and treatment protocols and the facility's procedures for obtaining drugs for PEP (63).

# **Exposure Reporting**

The prompt reporting of exposures is important, not only for management of the exposure but also for identification of workplace hazards and evaluation of preventive measures. Reporting systems should include ready access to expert consultants as well as safeguards to protect the confidentiality of the exposed worker. Unfortunately, a significant proportion of percutaneous injuries are not reported to hospital surveillance systems (range, 5 to 60%) (59, 129, 177, 183, 204). Timely and complete reporting of exposures can be facilitated by education of HCWs and a supportive, nonpunitive response by employers. HCW education, including orientation and in-service programs, should familiarize HCWs with their personal risk of occupational blood-borne pathogen exposure, measures to prevent such exposures, and the principles of postexposure management. HCWs must understand the importance of reporting exposures immediately after they occur, since certain indicated interventions (e.g., PEP for HIV and HBV) must be initiated promptly to be effective (38, 50, 114).

#### **Exposure Assessment and Emergency Management**

Upon reporting an exposure, the HCW should be evaluated and counseled regarding the risk of blood-borne pathogen infection, the potential usefulness of PEP for HIV and/or HBV, the need for follow-up evaluation, and precautions to prevent possible HIV transmission to others during the follow-up period (50). Risk evaluation should include an assessment of factors that may increase or decrease the probability of infection transmission.

First aid, if necessary, should be administered as quickly as possible. Puncture wounds and other cutaneous injury sites should be washed with soap and water, and exposed oral and nasal mucous membranes should be vigorously flushed with water. Eyes should be irrigated with clean water, saline, or sterile irrigants (50, 115). Although there is no evidence that antiseptics for wound care reduce the risk of blood-borne pathogen transmission, their use is not contraindicated. The use of bleach or other caustic agents that cause local tissue trauma is not recommended (38).

After any exposure, efforts should be made to identify and evaluate clinically and epidemiologically the source patient for evidence of HIV, HBV, and/or HCV infection. The source patient should be informed of the incident and consent should be obtained for HIV, HBV, and HCV testing.

The circumstances of the exposure should be recorded in a

confidential medical record. Data collection should include demographic information about the exposed worker, details about the exposure itself (including date, time, job duty being performed, type of exposure, amount and type of fluid or material involved, type of device used, and severity of exposure), a description of infection control precautions used, information about the source patient, and details about postexposure management, counseling, and follow-up (50, 114).

#### Postexposure Chemoprophylaxis for HIV

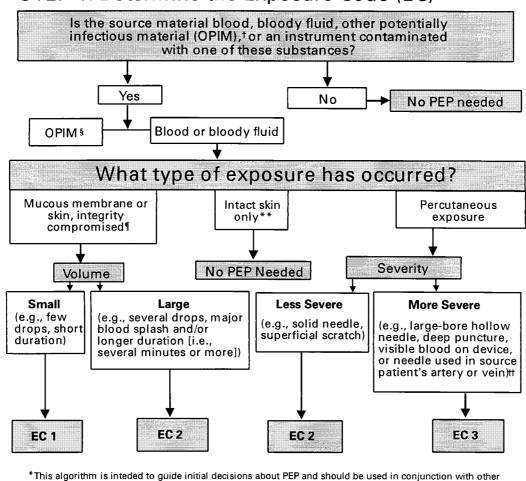
**Background.** Information from a retrospective case-control study of HCWs from France, the United Kingdom, and the United States suggesting that ZDV PEP may reduce the risk for HIV transmission after occupational exposure to HIV-infected blood (55), along with data on ZDV efficacy in preventing perinatal transmission (81) and evidence that PEP prevented or ameliorated retroviral infection in some studies in animals (27), prompted the Public Health Service (PHS) to publish a statement on management of occupational exposures to HIV in 1996 (57). The PHS subsequently published expanded and updated recommendations for occupational HIV exposure management for HCWs in May 1998 (63). These guidelines have been supported by groups such as the International AIDS Society—USA (42).

ZDV and other reverse transcriptase inhibitors may be important for PEP by preventing early viral dissemination. Studies of HIV-infected patients have shown that other antiretroviral agents, such as the reverse transcriptase inhibitor lamivudine, and the class of protease inhibitors that includes saquinavir and indinavir (IDV) significantly decrease plasma HIV levels, especially when used in combination with ZDV (100). Protease inhibitors may be useful for prophylaxis based on the site of activity in the replication cycle (i.e., after viral integration has occurred) in addition to demonstrated effectiveness in reducing viral load.

Animal studies. PEP has prevented or ameliorated retroviral infection in some studies with animals, particularly when it was administered soon after exposure (199, 230, 242, 251, 262). However, the application of animal studies, especially those using nonhuman retroviruses, is uncertain. In addition to the use of nonhuman retroviruses, many variables, such as viral inoculum size, antiretroviral dose, administration route, time to onset of treatment, and dose interval, may influence the apparent effectiveness of the treatment under study (27).

**Human studies.** There are few data with which to assess the efficacy of PEP in humans. The optimal study design for determining the efficacy of ZDV for PEP would be a prospective, placebo-controlled trial. However, this has not been possible because of the requirement for a large number of HCWs and the relatively low rate of HIV seroconversion following occupational exposure (S. W. LaFon, B. D. Mooney, J. P. Mc-Cullen, K. H. Pattishall, M. L. Smiley, M. D. Rodgers, and S. N. Lehrman, Program Abstr. 30th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 489, 1990). In the absence of such a trial, other sources of data have been used to assess the use of ZDV for PEP.

In a multicenter, double-blind, placebo-controlled clinical trial of ZDV to prevent perinatal HIV transmission, ZDV therapy was associated with a 67.5% reduction in the risk of mother-to-infant HIV transmission (53). The protective effect of ZDV was only partly explained by reduction of the HIV titer in maternal blood, suggesting a possible direct prophylactic effect of ZDV (248). Additionally, a recent placebo-controlled study in Thailand showed that a short-term antenatal regimen of ZDV reduced the risk for perinatal HIV transmission by



STEP 1: Determine the Exposure Code (EC)

guidance provided in this report.

<sup>†</sup>Semen or vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, or amniotic fluids; or tissue.

<sup>§</sup>Exposures to OPIM must be evaluated on a case-by-case basis. In general, these body substances are considered a low risk for transmission in health-care settings. Any unprotected contact to concentrated HIV in a research laboratory or production facility is considered an occupational exposure that requires clinical evaluation to determine the need for PEP.

Skin integrity is considered compromised if there is evidence of chapped skin, dermatitis, abrasion, or open wound.

\*\*Contact with intact skin is not normally considered a risk for HIV transmission. However, if the exposure was to blood, and the circumstance suggests a higher volume exposure (e.g., an extensive area of skin was exposed or there was prolonged contact with blood), the risk for HIV transmission should be considered.

<sup>††</sup> The combination of these severity factors (e.g., large-bore hollow needle and deep puncture) contribute to an elevated risk for transmission if the source person is HIV-positive.

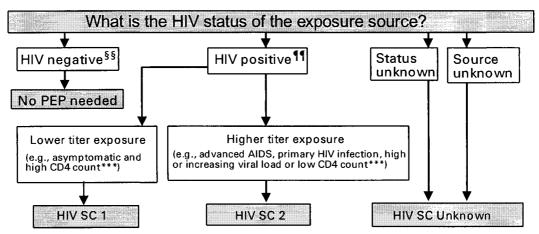
FIG. 1. Determining the need for HIV PEP after an occupational exposure. This algorithm is intended to provide guidance for occupational exposures to blood, fluid containing visible blood, or other potentially infectious fluid or tissue through a percutaneous injury or through contact with a mucous membrane or nonintact skin. Follow steps 1 through 3 to determine the PEP recommendation. Adapted from reference 63.

51% (62). Also, the CDC retrospective case-control study found that PEP with ZDV was associated with a decrease of approximately 81% in the risk for HIV seroconversion among HCWs who had a percutaneous exposure to HIV-infected blood (39).

However, any protection afforded is not absolute. Failure of ZDV PEP to prevent HIV infection in HCWs has been reported (156, 174; G. Weisburd, J. Biglione, M. M. Arbulu, J. C. Terrazzino, and A. Pesiri, Program Abstr. XI Int. Conf. AIDS, abstr. pub. C. 1141, 1996). Additional failures of ZDV PEP have been described among individuals exposed to an inoculum of HIV-infected blood larger than what would be expected

from a needlestick. These non-HCW cases included one blood transfusion, one suicidal self-inoculation, one assault with a needle-syringe, and two instances of accidental intravenous infusion of HIV-infected blood components during nuclear medicine procedures (156). Possible factors that may have contributed to the apparent failures in these instances include exposure to a ZDV-resistant strain of HIV, a high-titer and/or large-inoculum exposure, delayed initiation and/or short duration of PEP, and possible factors related to the host (e.g., cellular immune system responsiveness) and/or to the source patient's virus (e.g., presence of syncytium-forming strains) (63).

# STEP 2: Determine the HIV Status Code (HIV SC)



- §§ A source is considered negative for HIV infection if there is laboratory documentation of a negative HIV antibody, HIV polymerase chain reaction (PCR), or HIV p24 antigen test result from a specimen collected at or near the time of exposure and there is no clinical evidence of recent retroviral-like illness.
- 11 A source is considered infected with HIV (HIV positive) if there has been a positive laboratory result for HIV antibody, HIV PCR, or HIV p24 antigen or physician-diagnosed AIDS.
- \*\*\* Examples are used as surrogates to estimate the HIV titer in an exposure source for purposes of considering PEP regimens and do not reflect all clinical situations that may be observed. Although a high HIV titer (HIV SC 2) in an exposure source has been associated with an increased risk for transmission, the possibility of transmission from a source with a low HIV titer also must be considered.

# STEP 3: Determine the PEP Recommendation

# EC HIV SC PEP recommendation

- 1 1 **PEP may not be warranted.** Exposure type does not pose a known risk for HIV transmission. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician.
- 1 2 **Consider basic regimen.**<sup>†††</sup>Exposure type poses a negligible risk for HIV transmission. A high HIV titer in the source may justify consideration of PEP. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician.
- 2 1 Recommend basic regimen. Most HIV exposures are in this category; no increased risk for HIV transmission has been observed but use of PEP is appropriate.
- 2 2 Recommend expanded regimen.<sup>§§§</sup> Exposure type represents an increased HIV transmission risk.
- 3 1 or 2 **Recommend expanded regimen.** Exposure type represents an increased HIV transmission risk.
- Unknown If the source or, in the case of an unknown source, the setting where the exposure occurred suggests a possible risk for HIV exposure and the EC is 2 or 3, consider PEP basic regimen.
- †††Basic regimen is four weeks of zidovudine, 600 mg per day in two or three divided doses, and lamivudine, 150 mg twice daily.
- §§§Expanded regimen is the basic regimen plus either indinavir, 800 mg every 8 hours, or nelfinavir, 750 mg three times a day.

FIG. 1-Continued.

**PHS recommendations for chemoprophylaxis.** Chemoprophylaxis should be recommended to exposed workers after occupational exposures associated with a known risk for HIV transmission, should be considered for exposures with a negligible risk, and may not be warranted for exposures that do not pose a known risk for HIV transmission (Fig. 1). For exposures

for which PEP is considered appropriate, exposed workers should be informed that (i) knowledge about the efficacy and toxicity of drugs used for PEP is limited; (ii) only ZDV has been shown to prevent HIV transmission in humans; (iii) there are no data to address whether adding other antiretroviral drugs provides any additional benefit for PEP, but some ex-

TABLE 7. Recommended served	logic testing for HCWs following	ng occupational exposures to HIV, HBV, and HCV	

Infection	Recommended serologic tests at:				
status of source patient	Baseline	6 wk	12 wk	6 mo	
HIV-positive	HIV antibody testing using EIA <sup>a</sup>	HIV antibody testing using EIA	HIV antibody testing using EIA	HIV antibody testing using EIA	
HBsAg- positive	Anti-HBs if previously vaccinated against HBV and response to vaccination unknown		-		
Anti-HCV- positive	HCV antibody testing using EIA <sup>b</sup> ; ALT measurement	HCV RNA (optional) <sup>c</sup>		HCV antibody testing (using EIA); ALT measurement at 4 to 6 mo <sup>c</sup>	
Unknown	HIV antibody testing using EIA; anti-HBs if previously vaccinated to HBV and response to vaccination unknown; HCV antibody testing using EIA; ALT measurement	HIV antibody testing using EIA	HIV antibody testing using EIA	HIV antibody testing using EIA; HCV antibody testing using EIA; ALT measurement	

<sup>a</sup> Confirmation by Western blot testing of all anti-HIV results reported as reactive by EIA.

<sup>b</sup> Confirmation by supplemental anti-HCV (i.e., recombinant immunoblot assay [RIBA]) testing of all anti-HCV results reported as repeatedly reactive by EIA.

<sup>c</sup> If earlier diagnosis of HCV infection is desired, testing for HCV RNA may be performed at 4 to 6 weeks.

perts recommend combination drug regimens because of increased potency and concerns about drug-resistant virus; (iv) data regarding toxicity of antiretroviral drugs in persons without HIV infection or who are pregnant are limited; and (v) any or all drugs for PEP may be declined by the exposed worker. HCWs who have HIV occupational exposures for which PEP is not recommended should be informed that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the type of exposure.

Most HIV exposures will warrant only a two-drug regimen, using two nucleoside analogue reverse transcriptase inhibitors, usually ZDV and lamivudine. The addition of a third drug, usually a protease inhibitor (i.e., IDV or nelfinavir), should be considered for exposures that pose an increased risk for transmission or when resistance to the other drugs used for PEP is known or suspected. ZDV-resistant strains of HIV can be transmitted and have been reported to cause primary infections (99; G. Ippolito, P. Del Poggio, C. Arici, G. P. Gregis, G. Antonelli, and E. Riva, Letter, JAMA 272:433-434, 1994). If the exposure source is unknown or the HIV status of the source patient cannot be tested, information about the circumstances of the exposure should be assessed to determine the risk for transmission of HIV. Certain situations, as well as the type of exposure, may suggest an increased or decreased risk; an important consideration is the prevalence of HIV in the population group (i.e., institution or community) from which the contaminated source material was derived. Decisions regarding appropriate management should be individualized based on the risk assessment (63).

PEP should be initiated as soon as possible (i.e., within hours of the exposure). The interval within which PEP should be started for optimal efficacy is not known. The optimal duration of PEP also is unknown. Because 4 weeks of ZDV appears sufficient to be protective in HCWs (39), PEP probably should be administered for 4 weeks, if tolerated. When PEP is used, drug toxicity monitoring should include a complete blood count and renal and hepatic chemical function tests at baseline and 2 weeks after starting PEP.

**Counseling and follow-up.** All HCWs with occupational exposure to HIV should receive follow-up counseling, postexposure testing (Table 7), and medical evaluation, regardless of whether they receive PEP. HIV antibody testing should be performed for at least 6 months postexposure (e.g., at 6 weeks, 12 weeks, and 6 months). HIV testing using EIA should be

performed on any HCW who has an illness that is compatible with an acute retroviral syndrome. HIV antibody testing using EIA should be used to monitor for seroconversion. The routine use of direct virus assays (e.g., PCR for HIV RNA) to detect infection in exposed HCWs generally is not recommended (34, 113, 114).

The psychological impact of an occupational HIV exposure may be considerable and should be addressed during counseling and follow-up (236). Experts have found that supportive counseling is an important part of management (98, 114, 135, 136). To prevent the possibility of further transmission to others, the HCW should be advised to refrain from donating blood, semen, or organs during the follow-up period and to refrain from breast-feeding when safe and effective alternatives are available. To prevent HIV transmission to sexual contacts, all exposed HCWs should abstain from, or use latex condoms during, sexual intercourse throughout the follow-up period, especially during the first 6 to 12 weeks after the exposure, when most HIV-infected persons are expected to seroconvert (63).

Toxicity. An important goal of PEP is to encourage and facilitate compliance with the prescribed regimen. Therefore, the toxicity profile of antiretroviral agents is a relevant consideration. All of the antiretroviral agents have been associated with side effects (63). Side effects associated with many of the nucleoside analogue reverse transcriptase inhibitors are chiefly gastrointestinal (e.g., nausea or diarrhea). Rare but serious side effects, such as seizures, have been reported with ZDV PEP (M. D'Silva, D. Leibowitz, and J. P. Flaherty, Letter, Lancet 346:452, 1995). The use of protease inhibitors has been associated with new onset of diabetes mellitus, hyperglycemia, diabetic ketoacidosis, and exacerbation of preexisting diabetes mellitus (266a; M. D. Dubé, D. L. Johnson, J. S. Cumer, and J. M. Leedon, Letter, Lancet 350:713-714, 1997). Nephrolithiasis has been associated with IDV use (including in HCWs using the drug for PEP) (S. A. Wang and the HIV PEP Registry Group, Program Abstr. Infect. Dis. Soc. Am. 35th Annu. Meet., abstr. 482, 1997); however, the incidence of this potential complication may be limited by drinking at least 48 oz (1.5 liters) of fluid per 24-h period (19). Rare cases of hemolytic anemia also have been associated with the use of IDV. Nelfinavir, saquinavir, and ritonavir have all been associated with the development of diarrhea; however, this side effect usually responds to treatment with antimotility agents that can be

Vaccination and antibody response status of exposed worker	Treatment when source is found to be:				
	HBsAg positive	HBsAg negative	Not tested or status unknown		
Unvaccinated	Treat with one dose of HBIG <sup>b</sup> and initiate HB vaccine <sup>c</sup>	Initiate HB vaccine series	Initiate HB vaccine series		
Previously vaccinated					
Known responder <sup>c</sup>	No treatment	No treatment	No treatment		
Known nonresponder	Treat with two doses of HBIG or one dose of HBIG and initiate revaccination	No treatment	If known high risk source, treat as if source were HBsAg positive		
Antibody response unknown	Test exposed person for anti-HBs (if adequate, no treatment; if inadequate, treat with one dose of HBIG and vaccine booster)	No treatment	Test exposed for anti-HBs (if adequate, no treatment; if inadequate, treat with vaccine booster and recheck titer in 1 to 2 mo)		

TABLE 8. Recommended PEP for percutaneous or permucosal exposure to HBV in the United States<sup>a</sup>

<sup>a</sup> Adapted from reference 60.

<sup>b</sup> HBIG, hepatitis B IG (dose, 0.06 ml/kg [intramuscularly]).

<sup>c</sup> Hepatitis B vaccine.

<sup>d</sup> A responder is defined as a person with adequate levels of anti-HBs in serum (i.e., anti-HBs is  $\geq 10 \text{ mIU/ml}$ ); inadequate response to vaccination defined as level of anti-HBs in serum of <10 mIU/ml.

prescribed for use, if necessary, at the time any one of these drugs is prescribed for PEP. The manufacturer's package insert should always be consulted for questions about potential drug interactions.

#### Postexposure Prophylaxis for HBV

PEP with hepatitis B vaccine and hepatitis B IG among persons susceptible to HBV is highly effective in preventing infection after an exposure. Management of HCWs after percutaneous (e.g., needlestick, laceration, or bite) or mucosal (e.g., mucous membrane or ocular) exposure to potentially infectious body fluids must include consideration of (i) the HBsAg status of the source of exposure and (ii) the hepatitis B vaccination and vaccine response status of the exposed HCW. The ACIP of the PHS and HICPAC have provided detailed advice on postexposure immunoprophylaxis (60). Table 8 provides a guide to recommended management for various HBV exposures. Ideally, immunoprophylaxis should be initiated as soon as possible after a percutaneous or permucosal exposure; its value beyond 7 days after exposure is unclear.

#### **Postexposure Management of HCV**

HCV prophylaxis. Several studies have attempted to assess the effectiveness of prophylaxis with IG for the prevention of posttransfusion NANB hepatitis. However, the results from these studies are difficult to compare and interpret because of lack of uniformity in diagnostic criteria, varied study designs (including some lacking blinding and control groups), and administration of the first dose of IG prior to rather than after exposure in all but one study (164, 231, 238). Data from these studies have not been reanalyzed since anti-HCV testing became available. Beginning in 1992, IG has been manufactured from plasma that has been screened for anti-HCV. Therefore, if protective antibody does exist, screening and removal of anti-HCV-positive units may reduce the effectiveness of IG as PEP for HCV. An experimental study conducted with chimpanzees found that IG with a high titer of anti-HCV administered 1 h after exposure to HCV did not prevent infection or disease (168).

In 1994, the ACIP reviewed the available data and concluded that there was no support for the use of IG as PEP for hepatitis C (7). The ACIP based its recommendation on the facts that (i) no protective antibody response has been identified following HCV infection, (ii) prior studies of IG use to prevent posttransfusion NANB hepatitis may not be relevant in making recommendations regarding postexposure prophylaxis for hepatitis C, and (iii) experimental studies with chimpanzees showed IG's lack of efficacy in preventing infection after exposure.

There have been no controlled studies assessing the effectiveness of antiviral agents (e.g., alpha interferon) for HCV PEP among HCWs. Although the specific mechanism of action is poorly understood, an established infection may need to be present for interferon to be effective (192, 216). Therefore, PEP with alpha interferon prior to demonstration of HCV infection is not recommended.

Substantial challenges exist in the development of an effective vaccine against HCV, including the significant heterogeneity of the HCV genome and the lack of protective immunity elicited by HCV in the host (222). The development of an effective vaccine against HCV awaits a better understanding of the molecular biology of and immune response to this virus.

Follow-up of HCWs after an occupational exposure to HCV. There is currently no effective PEP for HCV infection. In the absence of effective prophylaxis, persons who have been exposed to HCV may benefit from knowing their infection status so they can seek evaluation for chronic liver disease and treatment. The CDC recently issued recommendations that individual institutions implement policies and procedures for follow-up after percutaneous or permucosal exposure to anti-HCV-positive blood (64a). The purpose of follow-up testing is to address individual workers' concerns about their risk and outcome and to identify persons who might benefit from antiviral therapy. At a minimum, such policies should include (i) baseline testing of the source for anti-HCV, (ii) baseline and follow-up (e.g., at 4 to 6 months) testing of the exposed person for anti-HCV and ALT activity (Table 6) (if earlier diagnosis of HCV infection is desired, testing for HCV RNA may be performed at 4 to 6 weeks), (iii) confirmation by supplemental anti-HCV testing of all anti-HCV results reported as positive by EIA, and (iv) education of HCWs about the risk for and prevention of transmission of all blood-borne pathogens, including HCV, in occupational settings, with the information routinely updated to ensure accuracy.

While interferon has a proven efficacy in treating chronic hepatitis C, there is no specific therapy of proven benefit for acute hepatitis C (109). Several studies have suggested that

Occupation	Authors and reference	No. of patients tested	No. of patients HIV positive	No. of HIV-positive patients linked to HCWs
Family physician	Danila et al. (85)	325	0	
Dentist	Dickinson et al. (92)	900	5	0
Dentist	Jaffe et al. (150)	616	28	0
Surgeon	Mishu et al. (185)	1,279	1	0
Breast surgeon	Rogers et al. (228)	468	2	0
Orthopedic surgeon	von Reyn et al. (271)	1,174	2	0

TABLE 9. Retrospective studies of HCWs infected with HIV

early therapy with alpha interferon may be effective in preventing progression from acute to chronic disease (36, 200, 270). However, there are no data indicating that treatment begun early in the course of chronic infection is less effective than treatment begun in the acute phase of infection.

#### MANAGEMENT OF INFECTED HCWS

#### Transmission of HIV from Infected HCWs to Patients

There have been two reported instances of HIV transmission from HCWs to patients. In July 1990, the CDC reported a case of transmission of HIV from a Florida dentist to a patient during an invasive dental procedure (49). Subsequent epidemiologic investigation and molecular genetic sequencing identified five additional patients who were infected while receiving care from the dentist. Each of the six patients had no other identified risk factors for acquiring HIV, and each was infected by a strain of HIV that closely matched that of the dentist by genetic sequencing analysis. Although the specific incidents that resulted in HIV transmission to these patients are uncertain, evidence strongly supports dentist-to-patient rather than patient-to-patient transmission (72, 206). A second case, reported in 1997, involved an orthopedic surgeon in France, who probably became infected with HIV in 1983 and had performed surgical procedures on 3,004 persons since that time. An epidemiologic investigation found one person among these patients who was HIV seronegative before a prolonged surgical procedure performed by the surgeon in 1992 and who subsequently was HIV seropositive. No other risk factors were documented for the patient, and nosocomial transmission of HIV from the surgeon to the patient was confirmed by an evaluation of viral sequences from both persons (28).

Retrospective investigation data. Even before reports of the Florida dentist case were published, many health departments, hospitals, and other agencies were conducting investigations of HIV-infected HCWs and notifying patients who had received care from these providers. Retrospective studies of a number of HIV-infected dentists, surgeons, and physicians revealed no evidence of HCW-to-patient HIV transmission during patient care (Table 9). A summary of all published and unpublished investigations of which the CDC was aware through January 1995 showed no documented cases of HIV transmission among 22,171 patients treated by HIV-infected HCWs, including a breast surgeon, a general surgeon, two obstetrics and gynecology residents, two orthopedic surgeons, and several dentists (227). Epidemiologic and laboratory follow-up of 110 of the 113 identified seropositive patients showed that the majority (90 of 110 [82%]) were either documented as having been infected before receiving care from the infected HCW or had established risk factors for acquiring HIV; 15 did not have clearly established risks but had had opportunities for potential exposure to HIV; and five had no identified risk (227). Genetic sequence analysis was done on HIV strains from three HCWs

and 30 seropositive patients, including three of the five patients who had no identified risk and 13 of the 15 patients with potential but undocumented risks for exposure. In no instances were the viral strains of patients and HCWs found to be related (227). Although limited by the lack of complete availability of HIV test results, procedure records, and information about the stage of the HCW's HIV infection during the time the worker did procedures, these results are consistent with conclusions by the CDC and others that the risk of HIV transmission from HCWs to patients is very low (25, 52).

# Transmission of HBV from Infected HCWs to Patients

Since the introduction of serologic testing in the 1970s, there have been at least 46 reports worldwide of HBV-infected HCWs transmitting HBV to patients during invasive procedures (24). The number of patients infected by a single HCW ranged from 1 to more than 50. Most reports of HCWs transmitting HBV to patients occurred prior to the widespread use of barrier precautions in some HCW groups (e.g., gloves by dentists), and many have involved readily apparent deficiencies in infection control practices. Although clusters in which there were no apparent deficiencies have occasionally occurred, investigations indicate that when HCWs adhere to recommended infection control procedures the risk of HBV transmission from HCW to patient is low.

A combination of factors is believed to be responsible for HBV transmission from HCWs to patients (52). One factor associated with increased risk of transmission is the HCW being HBeAg positive, indicating a higher level of infectivity (137, 138, 217, 218, 221, 275). In the United Kingdom, several episodes of HBeAg-negative surgeons transmitting HBV have been reported (127, 128, 145, 250). These surgeons were found to be carriers of a precore mutant strain of HBV that prevents expression of HBeAg but allows the expression of infectious virus. No such transmission has been reported from other parts of Europe or Japan, where the frequency of this strain appears more common (31, 201), or from the United States, where the frequency of this strain is unknown. Other factors believed to be responsible for HBV transmission from infected HCWs to patients include contamination of surgical wounds or traumatized tissue either from unintentional injury to the HCW during invasive procedures and/or a major break in standard infection control practices (e.g., not wearing gloves during an invasive procedure).

Clusters of HBV transmission from HCW to patient have been reported even when deficiencies of surgical technique or infection control practice could not be identified. In 1991, an HBeAg-positive cardiothoracic surgeon was determined to have transmitted HBV to 19 (13%) of 142 patients (132). In a simulation in which the surgeon tied surgical knots continuously for 1 h, visible skin separations were observed on his index fingers and HBsAg was detected in the saline used to rinse out his gloves. Whether these phenomena contributed to transmission is not clear.

# Transmission of HCV from Infected HCWs to Patients

There are no reported cases of HCV transmission from infected surgeons or dentists to patients in the United States. Worldwide, there are three reports of HCV transmission from infected health care providers (95, 101; P. Brown, News, Br. Med. J. **319**:1219, 1999). Between 1988 and 1993 in Spain, five patients developed acute HCV infection after undergoing heart valve replacement. On investigation, the cardiovascular surgeon was determined to have chronic hepatitis C and was implicated in the transmission of HCV to these patients (101). However, the factors responsible for transmission could not be identified.

In the United Kingdom, an HCW was found to be the probable source of infection during the investigation of a patient who developed acute HCV after cardiothoracic surgery (95). A retrospective investigation of 277 (91%) of the 304 other patients who had undergone invasive procedures performed by this surgeon found no additional cases of transmission. A third case, also in the United Kingdom, involving HCV transmission to one patient from a gynecologist, is currently under investigation (P. Brown, News, Br. Med. J. **319**:1219, 1999).

The CDC also is aware of a retrospective investigation of an HCV-infected plastic surgeon whose infection was diagnosed during a routine physical examination. HCV testing of 85% of the surgeon's patients was performed more than 6 months after their surgeries. Although three patients had evidence of HCV infection as indicated by the presence of anti-HCV antibodies, no provider-to-patient transmission was detected. One of these patients was known to have anti-HCV antibody before surgery, and the other two (one of whom had a history of injection drug use) were infected with strains that had a viral genotype and/or serotype different from that of the surgeon's strain (CDC, unpublished data).

In summary, specific factors related to an increased likelihood of transmission from HCV-infected HCWs to patients have yet to be identified. Available data indicate that the risk of HCV transmission from an infected HCW to a patient is extremely low.

# Prevention of Infection Transmission from Infected HCWs to Patients

The CDC has looked for episodes of blood-borne virus transmission to patients in health care settings, and the accumulated data have shown that the overall risk of blood-borne virus transmission from infected health care providers to patients is very low and that those for HIV and HCV specifically are extremely low.

To minimize the risk of blood-borne pathogen transmission from HCWs to patients, all HCWs should adhere to standard precautions, including the appropriate use of hand washing, protective barriers, and care in the use and disposal of needles and other sharp instruments (52). Technique changes and safer needle devices that potentially reduce percutaneous injury and recontact rates during surgery may also help reduce risks (256). Currently available data provide no basis for recommendations to restrict the practice of HCWs infected with HIV, HBV, or HCV who perform duties or procedures not identified as exposure-prone, provided the infected HCWs practice recommended surgical or dental technique and comply with standard precautions and current recommendations for sterilization and disinfection (52). **Prevention of HIV and HBV transmission during invasive procedures.** The CDC has characterized exposure-prone procedures as those that include digital palpation of a needle tip in a body cavity or the simultaneous presence of the HCW's fingers and a needle or other sharp instrument or object in a poorly visualized or highly confined anatomic site. During these procedures the routine use of gloves may not prevent injuries caused by sharp instruments and does not eliminate the potential for exposure of a patient to the HCW's blood.

To minimize the risk of HIV and HBV transmission from infected HCWs to patients during invasive procedures, the CDC issued recommendations in 1991 (52). HCWs who perform exposure-prone invasive procedures and who do not have serologic evidence of immunity to HBV from vaccination or previous infection should know their HBsAg status (and, if positive, their HBeAg status). HCWs who are infected with HBV and are HBeAg positive and HCWs who are infected with HIV should not perform exposure-prone procedures unless they have sought counsel from an expert review panel and been advised under what circumstances, if any, they may continue to perform these procedures. Such circumstances would include notifying prospective patients of the HCW's seropositivity before they undergo exposure-prone invasive procedures.

Since these recommendations have been issued, there has been no report of HIV transmission and only one report of HBV transmission from an infected HCW to patients in the United States (132).

**HCWs with blood-borne viruses.** The Society for Healthcare Epidemiologists of America has recently issued guidelines that include recommendations for management of HCWs infected with HIV, HBV, and HCV (3). Specifically, the society recommended that all HCWs use double gloving for procedures and that infected providers not be excluded from any aspect of patient care unless epidemiologically incriminated in the transmission of infections despite adequate precautions. The American College of Surgeons has stated that surgeons infected with HBV and HCV have no reason to alter their practice but should seek expert advice and appropriate treatment to prevent chronic liver disease (16).

No episode of HCV transmission from an infected HCW to a patient during surgical or dental care procedures has been observed in the United States. The CDC does not recommend restriction of HCWs with hepatitis C from performing invasive procedures.

### CONCLUSION

Future directions in the area of management of blood-borne pathogen infections in HCWs include more systematic surveillance of occupationally acquired HIV, HBV, and HCV infection; better definition of the epidemiology of blood contact and the efficacy of preventive measures; development and evaluation of new safety devices and protective barriers; evaluation of PEP; and development and evaluation of vaccines for HIV and HCV.

A sustained commitment to the occupational health of HCWs will ensure maximum protection for HCWs and patients and the availability of optimal medical care for all who need it.

#### REFERENCES

- Adams, K. S., C. L. Zehrer, and W. Thomas. 1993. Comparison of a needleless system with conventional heparin locks. Am. J. Infect. Control 21:263–269.
- Agerton, T. B., F. J. Mahoney, L. B. Polish, and C. N. Shapiro. 1995. Impact of the bloodborne pathogens standard on vaccination of healthcare workers with hepatitis B vaccine. Infect. Control Hosp. Epidemiol. 16:287–291.

- AIDS/TB Committee of the Society for Healthcare Epidemiology of America. 1997. Management of healthcare workers infected with hepatitis B virus, hepatitis C virus, human immunodeficiency virus, or other bloodborne pathogens. Infect. Control Hosp. Epidemiol. 18:349–363.
- Alter, H. J., P. V. Holland, R. H. Purcell, J. J. Lander, S. M. Feinstone, A. G. Morrow, and P. J. Schmidt. 1972. Posttransfusion hepatitis after exclusion of commercial and hepatitis B antigen-positive donors. Ann. Intern. Med. 77:691–699.
- Alter, H. J., L. B. Seeff, P. M. Kaplan, V. J. McAuliffe, E. C. Wright, J. L. Gerin, R. H. Purcell, P. V. Holland, and H. J. Zimmerman. 1976. Type B hepatitis: the infectivity of blood positive for e antigen and DNA polymerase after accidental needlestick exposure. N. Engl. J. Med. 295:909–913.
- Alter, M. J. 1993. The detection, transmission, and outcome of hepatitis C virus infection. Infect. Agents Dis. 2:155–166.
- Alter, M. J. 1994. Occupational exposure to hepatitis C virus: a dilemma. Infect. Control Hosp. Epidemiol. 15:742–744.
- Alter, M. J. 1994. Review of serologic testing for hepatitis C virus infection and risk of posttransfusion hepatitis C. Arch. Pathol. Lab. Med. 118:342– 345.
- Alter, M. J. 1995. Epidemiology of hepatitis C in the West. Semin. Liver Dis. 15:5–14.
- Alter, M. J. 1997. The epidemiology of acute and chronic hepatitis C. Clin. Liver Dis. 1:559–568.
- Alter, M. J., J. Ahtone, and J. E. Maynard. 1983. Hepatitis B virus transmission associated with a multiple-dose vial in a hemodialysis unit. Ann. Intern. Med. 99:330–333.
- Alter, M. J., R. J. Gerety, L. Smallwood, R. E. Sampliner, E. Tabor, F. Deinhardt, G. Frosner, and G. M. Matanoski. 1982. Sporadic non-A, non-B hepatitis: frequency and epidemiology in an urban United States population. J. Infect. Dis. 145:886–893.
- Alter, M. J., D. Kruszon-Moran, D. V. Nainan, G. M. McQuillan, F. Gao, L. A. Moyer, R. A. Kaslow, and H. S. Margolis. 1999. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. N. Engl. J. Med. 341:556–562.
- 14. Alter, M. J., H. S. Margolis, K. Krawczynski, F. N. Judson, A. Mares, W. J. Alexander, P. Y. Hu, J. K. Miller, M. A. Gerber, R. E. Sampliner, E. L. Meeks, and M. J. Beach for the Sentinel Counties Chronic Non-A Non-B Hepatitis Study Team. 1992. Natural history of community-acquired hepatitis C in the United States. N. Engl. J. Med. 327:1899–1905.
- Alter, M. J., and E. E. Mast. 1994. The epidemiology of viral hepatitis in the United States. Gastroenterol. Clin. N. Am. 23:437–455.
- American College of Surgeons. 1999. Statement on the surgeon and hepatitis. Bull. Am. Coll. Surg. 84:21–24.
- Anonymous. 1976. Relation of e antigen to infectivity of HBsAg-positive inoculations among medical personnel. Lancet ii:492–494.
- 18. Reference deleted.
- Anonymous. 1996. New drugs for HIV infection. Med. Lett. Drugs Ther. 38:35–37.
- Assogba, U., R. A. Ancelle Park, M. A. Rey, A. Barthelemy, J. Rottembourg, and J. C. Gluckman. 1988. Prospective study of HIV1 seropositive patients in hemodialysis centers. Clin. Nephrol. 29:312–314.
- Beekman, S. E., D. Vlahow, D. E. Koziol, E. D. McShalley, and J. M. Schmitt. 1994. Temporal association between implementation of universal precautions and a sustained, progressive decrease in percutaneous exposures to blood. Clin. Infect. Dis. 18:562–569.
- Bell, D. M. 1991. Human immunodeficiency virus transmission in health care settings: risk and risk reduction. Am. J. Med. 91(Suppl. 3B):294–300.
- Bell, D. M. 1997. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. Am. J. Med. 102(Suppl. 5B): 9–14.
- Bell, D. M., C. N. Shapiro, C. Ciesielski, and M. E. Chamberland. 1995. Preventing bloodborne pathogen transmission from health-care workers to patients. Surg. Clin. N. Am. 75:1189–1203.
- 25. Bell, D. M., C. N. Shapiro, D. H. Culver, W. J. Martone, J. W. Curran, and J. M. Hughes. 1992. Risk of hepatitis B and human immunodeficiency virus transmission to a patient from an infected surgeon due to percutaneous injury during an invasive procedure: estimates based on a model. Infect. Agents Dis. 1:263–269.
- Bennett, N. T., and R. J. Howard. 1994. Quantity of blood inoculated in a needlestick injury from suture needles. J. Am. Coll. Surg. 178:107–110.
- Black, R. J. 1997. Animal studies of prophylaxis. Am. J. Med. 102(Suppl. 5B):39–44.
- Blanchard, A., S. Ferris, S. Chamaret, D. Guétard, and L. Montagnier. 1998. Molecular evidence for nosocomial transmission of human immunodeficiency virus from a surgeon to one of his patients. J. Virol. 72:4537– 4540.
- Bond, W. W., M. S. Favero, N. J. Petersen, and J. W. Ebert. 1983. Inactivation of hepatitis B virus by intermediate-to-high-level disinfectant chemicals. J. Clin. Microbiol. 18:535–538.
- Bowden, F. J., B. Pollett, F. Birrell, and E. M. Dar. 1993. Occupational exposure to the human immunodeficiency virus and other bloodborne pathogens: a six year prospective study. Med. J. Aust. 158:810–812.

- Boxall, E. H., and A. Ballard. 1997. Fifth of e antigen negative carriers of hepatitis B virus should not perform exposure prone procedures. Br. Med. J. 314:144.
- 32. Bradley, D. W., K. Krawczynski, M. J. Beach, and M. A. Purdy. 1991. Non-A, non-B hepatitis: toward the discovery of hepatitis C and E viruses. Semin. Liver Dis. 11:128–146.
- Bukh, J., R. H. Miller, and R. H. Purcell. 1995. Genetic heterogeneity of hepatitis C virus: quasispecies and genotypes. Semin. Liver Dis. 15:41–63.
- Busch, M. P., and G. A. Satten. 1997. Time course of viremia and antibody seroconversion following human immunodeficiency virus exposure. Am. J. Med. 102(Suppl. 5B):117–124.
- Callender, M. E., Y. S. White, and R. Williams. 1982. Hepatitis B virus infection in medical and health care personnel. Br. Med. J. 284:324–326.
- Camma, C., P. Almasio, and A. Craxi. 1996. Interferon as treatment for acute hepatitis C: a meta-analysis. Dig. Dis. Sci. 41:1248–1255.
- 37. Reference deleted.
- Cardo, D. M., K. G. Castro, J. A. Polder, and D. M. Bell. 1994. Management of occupational exposure to HIV, p. 361–375. *In G.* Schochetman and J. R. George (ed.), AIDS testing: a comprehensive guide to technical, medical, social, legal, and management issues, 2nd ed. Springer-Verlag, New York, N.Y.
- 39. Cardo, D. M., D. H. Culver, C. A. Ciesielski, P. U. Srivastava, R. Marcus, D. Abiteboul, J. Heptonstall, G. Ippolito, F. Lot, P. McKibben, D. M. Bell, and the Centers for Disease Control and Prevention Needlestick Surveillance Group. 1997. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. N. Engl. J. Med. 337:1485–1490.
- Carman, W. F. 1997. The clinical significance of surface antigen variants of hepatitis B virus. J. Viral Hepatitis 4(Suppl. 1):11–20.
- Carman, W. F., F. J. Van Deursen, L. T. Mimms, D. Hardie, R. Coppola, R. Decker, and R. Sanders. 1997. The prevalence of surface antigen variants of hepatitis B virus in Papua New Guinea, South Africa, and Sardinia. Hepatology 26:1658–1666.
- 42. Carpenter, C. C. J., M. A. Fischl, S. M. Hammer, M. S. Hirsch, D. M. Jacobsen, D. A. Katzenstein, J. S. G. Montaner, D. D. Richman, M. S. Saag, R. T. Schooley, M. A. Thompson, S. Vella, P. G. Yeni, and P. A. Bolberding. 1998. Antiretroviral therapy for HIV infection in 1998: updated recommendations of the International AIDS Society—USA panel. JAMA 280:78–86.
- Center for Disease Control. 1977. Hepatitis—control measures for hepatitis B in dialysis centers. HEW publication no. [CDC] 78-8358 (Viral Hepatitis Investigations and Control Series). Center for Disease Control, Atlanta, Ga.
- 44. Center for Disease Control. 1978. Lack of transmission of hepatitis B to humans after oral exposure to hepatitis B surface antigen-positive saliva. Morbid. Mortal. Weekly Rep. 27:247–248.
- Centers for Disease Control. 1982. Recommendation of the Immunization Practices Advisory Committee (ACIP)—inactivated hepatitis B virus vaccine. Morbid. Mortal. Weekly Rep. 31:317–322, 328.
- Centers for Disease Control. 1987. Recommendations for prevention of HIV transmission in health-care settings. Morbid. Mortal. Weekly Rep. 36(2S):1S–18S.
- Centers for Disease Control. 1988. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. Morbid. Mortal. Weekly Rep. 37:377–382, 387–388.
- Centers for Disease Control. 1989. Guidelines for prevention of transmission of human immunodeficiency virus and hepatitis B virus to health-care and public safety workers. Morbid. Mortal. Weekly Rep. 38(Suppl. 6):1–37.
- Centers for Disease Control. 1990. Possible transmission of human immunodeficiency virus to a patient during an invasive dental procedure. Morbid. Mortal. Weekly Rep. 39:489–493.
- Centers for Disease Control. 1990. Public Health Service statement on management of occupational exposure to human immunodeficiency virus, including considerations regarding zidovudine postexposure use. Morbid. Mortal. Weekly Rep. 39(RR-1):1–14.
- Centers for Disease Control. 1991. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). Morbid. Mortal. Weekly Rep. 40(RR-13):1– 25.
- Centers for Disease Control. 1991. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. Morbid. Mortal. Weekly Rep. 40(RR-8):1–9.
- Centers for Disease Control and Prevention. 1994. Zidovudine for the prevention of HIV transmission from mother to infant. Morbid. Mortal. Weekly Rep. 43:285–287.
- Centers for Disease Control and Prevention. 1995. Hepatitis surveillance report, Atlanta, p. 3–6. Centers for Disease Control and Prevention, Atlanta, Ga.
- 55. Centers for Disease Control and Prevention. 1995. Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood—France, United Kingdom, and United States, January

1988-August 1994. Morbid. Mortal. Weekly Rep. 44:929-933.

- Centers for Disease Control and Prevention. 1996. Outbreaks of hepatitis B virus infection among hemodialysis patients—California. Morbid. Mortal. Weekly Rep. 45:285–289.
- Centers for Disease Control and Prevention. 1996. Update: provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. Morbid. Mortal. Weekly Rep. 45:467–472.
- Centers for Disease Control and Prevention. 1997. Evaluation of blunt suture needles in preventing percutaneous injuries among health-care workers during gynecologic surgical procedures—New York City, March 1993–June 1994. Morbid. Mortal. Weekly Rep. 46:25–29.
- Centers for Disease Control and Prevention. 1997. Evaluation of safety devices for preventing percutaneous injuries among health-care workers during phlebotomy procedures—Minneapolis-St. Paul, New York City, and San Francisco, 1993–1995. Morbid. Mortal. Weekly Rep. 46:20–25.
- 60. Centers for Disease Control and Prevention. 1997. Immunization of healthcare workers: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infections Control Practices Advisory Committee (HICPAC). Morbid. Mortal. Weekly Rep. 46(RR-18):23.
- Centers for Disease Control and Prevention. 1997. Recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. Morbid. Mortal. Weekly Rep. 46:603–606.
- Centers for Disease Control and Prevention. 1998. Administration of zidovudine during late pregnancy and delivery to prevent perinatal HIV transmission—Thailand, 1996–1998. Morbid. Mortal. Weekly Rep. 47:151– 154.
- 63. Centers for Disease Control and Prevention. 1998. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. Morbid. Mortal. Weekly Rep. 47(RR-7):1–34.
- Centers for Disease Control and Prevention. 1998. Recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. Morbid. Mortal. Weekly Rep. 47:603–606.
- 64a.Centers for Disease Control and Prevention. 1998. Recommendations for the prevention and control of hepatitis C virus (HCV) infection and HCVrelated chronic disease. Morbid. Mortal. Weekly Rep. 47(RR-19):1–39.
- Centers for Disease Control and Prevention. 1999. HIV/AIDS surveillance report, vol. 11, no. 1. Centers for Disease Control and Prevention, Atlanta, Ga.
- 66. Chamberland, M. E., L. R. Petersen, V. P. Munn, C. R. White, E. S. Johnson, M. P. Busch, A. J. Grindon, H. Kamel, P. M. Ness, A. W. Shafer, and G. Zeger. 1994. Human immunodeficiency virus infection among health care workers who donate blood. Ann. Intern. Med. 121:269–273.
- Chan, T. M., A. S. Lok, I. K. Cheng, and R. T. Chan. 1993. Prevalence of hepatitis C virus infection in hemodialysis patients: a longitudinal study comparing the results of RNA and antibody assays. Hepatology 17:5–8.
- Charache, P., J. L. Cameron, A. W. Maters, and E. I. Frantz. 1991. Prevalence of infection with human immunodeficiency virus in elective surgery patients. Ann. Surg. 214:562–568.
- 69. Reference deleted.
- Cheynier, R., P. Langlade-Demoyen, M.-R. Marescot, S. Blanhe, G. Boudin, S. Wain-Hobson, C. Griscelli, E. Vilmer, and F. Plata. 1992. Cytotoxic T lymphocyte responses in the peripheral blood of children born to human immunodeficiency virus-1-infected mothers. Eur. J. Immunol. 22:2211– 2217.
- Chirgwin, K., T. K. S. Rao, and S. H. Landesman. 1989. HIV infection in a high prevalence hemodialysis unit. AIDS 3:731–735.
- 72. Ciesielski, C., D. Marianos, C.-Y. Ou, R. Dombaugh, J. Witte, R. Berkelman, B. Gooch, G. Myers, C.-C. Luo, G. Schochetman, J. Howell, A. Lasch, K. Bell, N. Economou, B. Scott, L. Furman, J. Curran, and H. Jaffe. 1992. Transmission of human immunodeficiency virus in a dental practice. Ann. Intern. Med. 116:798–805.
- Ciesielski, C., and R. P. Metler. 1997. Duration of time between exposure and seroconversion in healthcare workers with occupationally acquired infection with human immunodeficiency virus. Am. J. Med. 102(Suppl. 5B):115–116.
- 74. Clerici, M., J. V. Giorgi, C.-C. Chou, V. K. Gudeman, J. A. Zack, P. Gupta, N. N. Ho, P. G. Nishanian, J. A. Berzofsky, and G. M. Shearer. 1992. Cell-mediated immune response to human immunodeficiency virus (HIV) type 1 in seronegative homosexual men with recent sexual exposure to HIV-1. J. Infect. Dis. 165:1012–1019.
- Clerici, M., J. M. Levin, H. A. Kessler, A. Harris, J. A. Berzofsky, A. L. Linday, and G. M. Shearer. 1994. HIV-specific T-helper activity in seronegative health care workers exposed to contaminated blood. JAMA 271: 42-46.
- Cleveland, J. L., B. Gooch, and S. A. Lockwood. 1997. Occupational blood exposures in dentistry: a decade in review. Infect. Control Hosp. Epidemiol. 18:717–721.
- Cleveland, J. L., S. A. Lockwood, B. F. Gooch, M. H. Mendelson, M. E. Chamberland, D. V. Valoui, S. L. Roistacher, J. M. Soloman, and D. W. Marianos. 1995. Percutaneous injuries in dentistry: an observational study. J. Am. Dent. Assoc. 126:745–751.

- Cleveland, J. L., C. Siew, S. A. Lockwood, S. E. Gruninger, B. F. Gooch, and C. N. Shapiro. 1996. Hepatitis B vaccination and infection among U.S. dentists, 1983–1992. J. Am. Dent. Assoc. 127:1385–1390.
- Collins, C. H., and D. A. Kennedy. 1987. Microbiological hazards of occupational needlestick and 'sharps' injuries. J. Appl. Bacteriol. 62:385–402.
- Comodo, N., F. Martinelli, E. De Majo, M. G. Colao, M. A. DiPietro, F. Manescalchi, M. Salvadori, and E. Lanciotti. 1988. Risk of HIV infection on patients and staff of two dialysis centers: seroepidemiological findings and prevention trends. Eur. J. Epidemiol. 4:171–174.
- 81. Connor, E. M., R. S. Sperling, R. Gelber, P. Kiselev, G. Scott, M. J. O'Sullivan, R. VanDyke, M. Bey, W. Shearer, R. L. Jacobson, E. Jimenez, E. O'Neill, B. Bazin, J.-F. Delfraissy, M. Culnane, R. Coombs, M. Elkins, J. Moye, P. Stratton, J. Balsley, and the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. 1994. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N. Engl. J. Med. 331:1173–1180.
- Cowan, D. N., J. F. Brundage, R. S. Pomerantz, R. N. Miller, and D. S. Burke. 1991. HIV infection among members of the US Army Reserve Components with medical and health occupations. JAMA 265:2826–2830.
- 83. Cuypers, H. T. M., D. Bresters, I. N. Winkel, H. W. Reesink, A. J. Weiner, M. Houghton, C. L. van der Poel, and P. N. Lelie. 1992. Storage conditions of blood samples and primer selection affect yield of cDNA polymerase chain reaction products of hepatitis C virus. J. Clin. Microbiol. 30:3320– 3324.
- 84. Reference deleted.
- 85. Danila, R. N., K. L. MacDonald, F. S. Rhame, M. Moen, D. O. Reier, J. C. LeTourneau, M. K. Sheehan, J. Armstrong, M. E. Bender, M. T. Osterholm, and the Investigation Team. 1991. A look-back investigation of patients of an HIV-infected physician: public health implications. N. Engl. J. Med. 325:1406–1411.
- Danzig, L. E., L. J. Short, K. Collins, M. Mahoney, S. Sepe, L. Bland, and W. R. Jarvis. 1995. Bloodstream infections associated with a needleless intravenous infusion system in patients receiving home infusion therapy. JAMA 273:1862–1864.
- Davis, G. L., J. Y. Lau, M. S. Urdea, P. D. Neuwald, J. C. Wilbur, and L. Corey. 1994. Quantitative detection of hepatitis C virus RNA with a solid-phase signal amplification method: definition of optimal conditions for specimen collection and clinical application in interferon-treated patients. Hepatology 19:1337–1341.
- Davis, G. L., and J. Y. N. Lau. 1995. Hepatitis C, p. 2082–2114. In W. S. Haubrich, F. Schaffner, and J. E. Berk (ed.), Gastroenterology, 5th ed. W. B. Saunders and Co., Philadelphia, Pa.
- Denes, A. E., J. L. Smith, J. E. Maynard, I. L. Doto, K. R. Berquist, and A. J. Finkel. 1978. Hepatitis B infection in physicians: results of a nationwide seroepidemiologic survey. JAMA 239:210–212.
- 90. Reference deleted.
- Di Bisceglie, A. M., G. M. Dusheiko, and M. C. Kew. 1985. Detection of markers of hepatitis B virus infection in urine of chronic carriers. J. Med. Virol. 16:337–341.
- Dickinson, G. M., R. E. Morhart, N. G. Klimas, C. I. Bandea, J. M. Laracuvente, and A. L. Bisno. 1993. Absence of HIV transmission from an infected dentist to his patients: an epidemiologic and DNA sequence analysis. JAMA 269:1802–1806.
- Dienstag, J. L., and D. M. Ryan. 1982. Occupational exposure to hepatitis B virus in hospital personnel: infection or immunization? Am. J. Epidemiol. 115:26–39.
- 94. Donegan, S. P., K. A. Steger, L. Recla, R. S. Huff, B. G. Werner, P. A. Rice, and D. E. Craven. 1992. Seroprevalence of human immunodeficiency virus in parturients at Boston City Hospital: implications for public health and obstetric practice. Am. J. Obstet. Gynecol. 167:622–629.
- Duckworth, G. J., J. Heptonstall, and C. Aitken. 1999. Transmission of hepatitis C virus from a surgeon to a patient. The Incident Control Team. Commun. Dis. Public Health 2:188–192.
- 96. Dusheiko, G. M., M. Smith, and P. J. Scheuer. 1990. Hepatitis C virus transmitted by human bite. Lancet 336:503–504.
- 97. Reference deleted.
- Elmslie, K., M. Ricketts, and L. Mulligan. 1990. Guidelines for counseling persons who have had an occupational exposure to human immunodeficiency virus. Can. Dis. Weekly Rep. 19(Suppl. 2):1–3.
- Erice, A., D. L. Mayers, D. G. Strike, K. J. Sannerud, F. E. McCutchan, K. Henry, and H. H. Balfour, Jr. 1993. Brief report: primary infection with zidovudine-resistant human immunodeficiency virus type 1. N. Engl. J. Med. 328:1163–1165.
- 100. Eron, J. J., S. L. Benoit, J. Jemsek, R. D. MacArthur, J. Santana, J. B. Quinn, D. R. Kuritzkes, M. A. Fallon, and M. Rubin. 1995. Treatment with lamivudine, zidovudine, or both in HIV-positive patients with 200 to 500 CD4+ cells per cubic millimeter. N. Engl. J. Med. 333:1662–1669.
- 101. Esteban, J. L., J. Gomez, M. Martell, B. Cabot, J. Quer, J. Camps, A. Gonzales, T. Otero, A. Moya, R. Estaban, and J. Guardia. 1996. Transmission of hepatitis C virus by a cardiac surgeon. N. Engl. J. Med. 334:555–560.
- 102. Fahey, B. J., D. E. Koziol, S. M. Banks, and D. K. Henderson. 1991. Frequency of nonparenteral occupational exposures to blood and body

fluids before and after universal precautions training. Am. J. Med. 90:145-153

- 103. Farci, P., H. J. Alter, D. Wong, R. H. Miller, J. W. Shih, B. Jett, and R. H. Purcell. 1991. A long-term study of hepatitis C virus replication in non-A, non-B hepatitis. N. Engl. J. Med. 325:98-104.
- 104. Favero, M. S. 1985. Sterilization, disinfection, and antisepsis in the hospital, p. 129-137. In E. H. Lennette, A. Balows, W. J. Hausler, Jr., and H. J. Shadomy (ed.), Manual of clinical microbiology, 4th ed. American Society for Microbiology, Washington, D.C.
- 105. Favero, M. S., and W. W. Bond. 1993. Disinfection and sterilization, p. 565-575. In A. J. Zuckerman and H. C. Thomas (ed.), Viral hepatitis: scientific basis and clinical management. Churchill Livingston, New York, N.Y.
- 106. Feinman, S. V., B. Berris, A. Rebane, J. C. Sinclair, S. Wilson, and D. Wrobel. 1979. Failure to detect hepatitis B surface antigen (HBsAg) in feces of HBsAg-positive persons. J. Infect. Dis. 140:407-410.
- 107. Flynn, N. M., S. M. Pollet, J. R. Van Horne, R. Elvebakk, S. D. Harper, and J. R. Carlson. 1987. Absence of HIV antibody among dental professionals exposed to infected patients. West. J. Med. 146:439-442.
- 108. Reference deleted.
- 109. Fried, M. W., and J. H. Hoofnagle. 1995. Therapy of hepatitis C. Semin. Liver Dis. 15:82-91.
- 110. Fujiyama, S., S. Kawano, S. Sato, M. Tanaka, M. Goto, Y. Taura, T. Sato, T. Kawahara, and K. Mizuno. 1992. Prevalence of hepatitis C virus antibodies in hemodialysis patients and dialysis staff. Hepatogastroenterology 39:161-165.
- 111. Garner, J. S., and the Hospital Infection Control Practices Advisory Committee. 1996. Guideline for isolation precautions in hospitals. Infect. Control Hosp. Epidemiol. 17:53-80.
- 112. Gartner, K. 1992. Impact of a needleless intravenous system in a university hospital. Am. J. Infect. Control 20:75-79
- 113. Gerberding, J. L. 1994. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and cytomegalovirus among health care personnel at risk for blood exposure: final report from a longitudinal study. J. Infect. Dis. **170**:1410–1417. 114. **Gerberding, J. L.** 1995. Management of occupational exposures to blood-
- borne viruses. N. Engl. J. Med. 332:444-451.
- 115. Gerberding, J. L., and D. K. Henderson. 1992. Management of occupational exposures to bloodborne pathogens: hepatitis B virus, hepatitis C virus, and human immunodeficiency virus. Clin. Infect. Dis. 14:1179-1185.
- 116. Gerberding, J. L., C. Littell, A. Tarkington, A. Brown, and W. P. Schecter. 1990. Risk of exposure of surgical personnel to patients' blood during surgery at San Francisco General Hospital. N. Engl. J. Med. 322:1788-1793.
- 117. Gershon, R. R. M., D. Vlahov, H. Farzedegan, and M. J. Alter. 1995. Occupational risk of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus infections among funeral service practitioners in Maryland. Infect. Control Hosp. Epidemiol. 16:194-197.
- 118. Goldman, M., C. Leisnard, J.-L. Vanherweghem, N. Dolle, C. Toussaint, S. Sprecher, J. Cogniaux, and L. Thiry. 1986. Markers of HTLV-III in patients with end stage renal failure treated by haemodialysis. Br. Med. J. 293:161-162.
- 119. Gordin, F. M., C. Gilbert, H. P. Hawley, and A. Willoughby. 1990. Prevalence of human immunodeficiency virus and hepatitis B virus in unselected hospital admissions: implications for mandatory testing and universal precautions. J. Infect. Dis. 161:14-17.
- 120. Grady, G. F., V. A. Lee, A. M. Prince, G. L. Gitnick, K. A. Fawaz, G. N. Vyas, M. D. Levitt, J. R. Senior, J. T. Galambos, T. E. Bynum, J. W. Singleton, B. F. Clowdus, K. Akdamar, R. D. Aach, E. I. Winkelman, G. M. Schiff, and T. Hersh. 1978. Hepatitis B immune globulin for accidental exposures among medical personnel: final report of a multicenter controlled trial. J. Infect. Dis. 138:625-638.
- 121. Gretch, D. R. 1997. Diagnostic tests for hepatitis C. Hepatology 26(Suppl. 1):43S-47S
- 122. Gretch, D. R., C. dela Rosa, R. L. Carithers, R. A. Wilson, K. Lindsav, R. P. Perrillo, and J. Albrecht. 1995. Assessment of hepatitis C viremia using molecular amplification technologies: correlations and clinical implications. Ann. Intern. Med. 123:321-329.
- 123. Gruninger, S. E., C. Siew, S.-B. Chang, R. Clayton, J. K. Leete, S. A. Hojvat, A. C. Verrusio, and E. A. Neidle. 1992. Human immunodeficiency virus type 1 infection among dentists. J. Am. Dent. Assoc. 123:57-64.
- 124. Guptan, R. C., V. Thakur, S. K. Sarin, K. Banerjee, and P. Khandekar. 1996. Frequency and clinical profile of precore and surface hepatitis B mutants in Asian-Indian patients with chronic liver disease. Am. J. Gastroenterol. 91:1312-1317.
- 125. Hadler, S. C., I. L. Doto, J. E. Maynard, J. Smith, B. Clark, J. Masley, T. Eikhoff, C. K. Himmelsbach, and W. R. Cole. 1985. Occupational risk of hepatitis B infection in hospital workers. Infect. Control 6:24-31.
- 126. Haiduven, D. J., T. M. Demaio, and D. A. Stevens. 1992. A five-year study of needlestick injuries: significant reduction associated with communication, education, and convenient placement of sharps containers. Infect. Control Hosp. Epidemiol. 13:265-271.

- 127. Halle, M. 1996. Patients want ban on operations by doctors with hepatitis B. Br. Med. J. 313:576.
- 128. Halle, M. 1996. Surgeon had mutant form of hepatitis B. Br. Med. J. **313:**771.
- 129. Hamory, B. H. 1983. Underreporting of needlestick injuries in a university hospital. Am. J. Infect. Control 11:174-177.
- 130. Hansen, M. E., G. L. Miller III, H. Redman, and D. D. McIntire. 1993. Needle-stick injuries and blood contacts during invasive radiologic procedures: frequency and risk factors. Am. J. Roentgenol. 160:1119-1122.
- 131. Hardy, N. M., S. Sandroni, S. Danielson, and W. J. Wilson. 1992. Antibody to hepatitis C virus increases with time on hemodialysis. Clin. Nephrol. 38:44-48.
- 132. Harpaz, R., L. Von Seidlein, F. M. Averhoff, M. P. Tormey, S. D. Sinha, K. Kotsopoulou, S. B. Lambert, B. H. Robertson, J. D. Cherry, and C. N. Shapiro. 1996. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. N. Engl. J. Med. 334:549-554.
- 133. Harris, J. R., R. F. Finger, J. M. Kobayashi, S. C. Hadler, B. L. Murphy, R. L. Berkelman, and K. E. Russell. 1984. The low risk of hepatitis B in rural hospitals: results of an epidemiologic survey. JAMA 252:3270-3272.
- 134. Hayashi, J., K. Nakashima, W. Kajiyama, A. Noguchi, M. Morofuji, Y. Maeda, and S. Kashiwaji. 1991. Prevalence of antibody to hepatitis C virus in hemodialysis patients. Am. J. Epidemiol. 134:651-657.
- 135. Henderson, D. K. 1991. Postexposure chemoprophylaxis for occupational exposure to human immunodeficiency virus type 1: current status and prospects for the future. Am. J. Med. 91(Suppl. 3B):312S-319S.
- Henderson, D. K., and J. L. Gerberding. 1989. Prophylactic zidovudine 136 after occupational exposure to human immunodeficiency virus: an interim analysis. J. Infect. Dis. 160:321-327.
- 137. Heptonstall, J. 1991. Outbreaks of hepatitis B virus infection associated with infected surgical staff. Dis. Rep. CDR Rev. 1:R81-R85.
- 138. Heptonstall, J. 1996. Lessons from two linked clusters of acute hepatitis B in cardiothoracic surgery patients. Dis. Rep. CDR Rev. 6:R119-R125.
- 139. Reference deleted.
- 140. Hernandez, M. E., M. Bruguera, T. Puyuelo, J. M. Barrera, J. M. Sanchez-Tapias, and J. Rodes. 1992. Risk of needlestick injuries in the transmission of hepatitis C virus in hospital personnel. J. Hepatol. 16:56-58.
- 141. Ho, D. D., T. Moudgil, and M. Alam. 1989. Quantitation of human immunodeficiency virus type 1 in the blood of infected persons. N. Engl. J. Med. 321:1621-1625.
- 142. Hoofnagle, J. H. 1995. Hepatitis B, p. 2062-2063. In W. S. Haubrich, F. Schaffner, and J. E. Berk (ed.), Gastroenterology, 5th ed. W. B. Saunders and Co., Philadelphia, Pa.
- 143. Hoofnagle, J. H., and A. M. Di Bisceglie. 1991. Serologic diagnosis of acute and chronic viral hepatitis. Semin. Liver Dis. 11:73-83.
- 144. Hsu, H. H., T. L. Wright, D. Luba, M. Martin, S. M. Feinstone, G. Garcia, and H. B. Greenberg. 1991. Failure to detect hepatitis C virus genome in human secretions with the polymerase chain reaction. Hepatology 14:763-767
- 145. Incident Investigation Team et al. 1997. Transmission of hepatitis B to patients from four infected surgeons without hepatitis B e antigen. N. Engl. J. Med. 336:178-184.
- 146. Reference deleted.
- 147. Ippolito, G., V. Puro, G. De Carli, and the Italian Study Group on Occupational Risk of HIV Infection. 1993. The risk of occupational human immunodeficiency virus infections in health care workers. Arch. Intern. Med. 153:1451-1458.
- 148. Reference deleted.
- 149. Irwin, G. R., A. M. Allen, W. H. Bancroft, J. J. Karwacki, H. L. Brown, R. H. Pinkerton, M. Wilhight, and F. H. Top, Jr. 1975. Hepatitis B antigen in saliva, urine, and stool. Infect. Immun. 11:142-145.
- 150. Jaffe, H. W., J. M. McCurdy, M. L. Kalish, T. Liberti, G. Metellus, B. H. Bowman, S. B. Richards, A. R. Neasman, and J. J. Witte. 1994. Lack of HIV transmission in the practice of a dentist with AIDS. Ann. Intern. Med. 121:855-859.
- 151. Jagger, J., E. H. Hunt, J. Brand-Elnagger, and R. D. Pearson. 1988. Rates of needle-stick injury caused by various devices in a university hospital. N. Engl. J. Med. 319:284-288.
- 152. Jagger, J., E. H. Hunt, and R. D. Pearson. 1990. Sharp object injuries in the hospital: causes and strategies for prevention. Am. J. Infect. Control 18: 227-231.
- 153. Janssen, R. S., M. E. St. Louis, G. A. Satten, S. E. Critchley, L. R. Petersen, R. S. Stafford, J. W. Ward, D. L. Hanson, N. Olivio, C. A. Schable, T. J. Dondero, and the Hospital HIV Surveillance Group. 1992. HIV infection among patients in U.S. acute care hospitals: strategies for the counseling and testing of hospital patients. N. Engl. J. Med. 327:445-452.
- 154. Jenison, S. A., S. M. Lemon, L. N. Baker, and J. E. Newbold. 1987. Quantitative analysis of hepatitis B virus DNA in saliva and semen of chronically infected homosexual men. J. Infect. Dis. 156:299-307.
- 155. Reference deleted.
- 156. Jochimsen, E. M. 1997. Failures of zidovudine post-exposure prophylaxis. Am. J. Med. 102(Suppl. 5B):52-55.

- 157. Kelen, G. D., T. DiGiovanna, L. Bisson, D. Kalainov, K. T. Sivertson, and T. C. Quinn. 1989. Human immunodeficiency virus infection in emergency department patients: epidemiology, clinical presentations, and risk to health care workers, the Johns Hopkins experience. JAMA 262:516–522.
- 158. Kelen, G. D., S. Fritz, B. Qaqish, R. Brookmeyer, J. L. Baker, R. L. Kline, R. M. Cuddy, T. K. Goessel, D. Floccare, K. A. Williams, K. T. Sivertson, S. Altman, and T. C. Quinn. 1988. Unrecognized human immunodeficiency virus infection in emergency department patients. N. Engl. J. Med. 318: 1645–1650.
- 159. Kelen, G. D., G. B. Green, R. H. Purcell, D. W. Chan, B. F. Qaqish, K. T. Sivertson, and T. C. Quinn. 1992. Hepatitis B and hepatitis C in emergency department patients. N. Engl. J. Med. 326:1399–1404.
- Kelker, H. C., M. Seidlin, M. Vogler, and F. T. Valentine. 1992. Lymphocytes from some long-term seronegative heterosexual partners of HIVinfected individuals proliferate in response to HIV antigens. AIDS 8:1355– 1359.
- 161. Kiyosawa, K., T. Sodeyama, E. Tanaka, Y. Nakano, S. Furuta, K. Nishioka, R. H. Purcell, and H. J. Alter. 1991. Hepatitis C in hospital employees with needlestick injuries. Ann. Intern. Med. 115:367–369.
- 162. Klein, R. S., K. Freeman, P. E. Taylor, and C. E. Stevens. 1991. Occupational risk for hepatitis C virus infection among New York City dentists. Lancet 339:1539–1542.
- 163. Klein, R. S., J. A. Phelan, K. Freeman, C. Schable, G. H. Friedland, N. Trieger, and N. H. Steigbigel. 1988. Low occupational risk of human immunodeficiency virus infection among dental professionals. N. Engl. J. Med. 318:86–90.
- Knodell, R. G., M. E. Conrad, A. L. Ginsberg, and C. J. Bell. 1976. Efficacy of prophylactic gamma-globulin in preventing non-A, non-B post-transfusion hepatitis. Lancet i:557–561.
- 165. Kobayashi, H., M. Tsuzuki, K. Koshimizu, H. Toyama, N. Yoshihara, T. Shikata, K. Abe, K. Mizuno, N. Otomo, and T. Oda. 1984. Susceptibility of hepatitis B virus to disinfectants and heat. J. Clin. Microbiol. 20:214–216.
- 166. Koretz, R. L., M. Brezina, A. J. Polito, S. Quan, J. Wilbur, R. Dinello, and G. Gitnick. 1993. Non-A, non-B posttransfusion hepatitis: comparing C and non-C hepatitis. Hepatology 17:361–365.
- 167. Reference deleted.
- 168. Krawczynski, K., M. J. Alter, and D. L. Tankersley. 1996. Effect of immune globulin on the prevention of experimental hepatitis C virus infection. J. Infect. Dis. 173:822–828.
- 169. Reference deleted.
- Langlade-Demoyen, P., N. Ngo-Giang-Huong, F. Ferchal, and E. Oksenhendler. 1994. Human immunodeficiency virus (HIV) *nef*-specific cytotoxic T lymphocytes in noninfected heterosexual contacts of HIV-infected patients. J. Clin. Investig. 93:1293–1297.
- 171. Laras, A., J. Koskinas, K. Avgidis, and S. J. Hadziyannis. 1998. Incidence and clinical significance of hepatitis B virus precore gene translation initiation mutations in e antigen-negative patients. J. Viral Hepatitis 5:241–248.
- 172. Lau, J. Y., M. Mizokami, J. A. Kolberg, G. L. Davis, L. E. Prescott, T. Ohno, R. P. Perrillo, K. L. Lindsay, R. G. Gish, K.-P. Qian, M. Kohara, P. Simmonds, and M. S. Urdea. 1995. Application of six hepatitis C virus genotyping systems to sera from chronic hepatitis C patients in the United States. J. Infect. Dis. 171:281–289.
- 173. Liang, T. J., K. Hasegawa, S. J. Munoz, C. N. Shapiro, B. Yoffe, B. J. McMahon, C. Feng, H. Bei, M. J. Alter, and J. L. Dienstag. 1994. Hepatitis B virus precore mutation and fulminant hepatitis in the United States: a polymerase chain reaction-based assay for the detection of specific mutation. J. Clin. Investig. 93:550–555.
- 174. Lot, F., and D. Abiteboul. 1995. Health-care workers infected with HIV in France as of June 30, 1995. Bull. Epidemiol. Hebd. 44:193–194.
- Louie, M., D. E. Low, and S. V. Feinman. 1992. Prevalence of bloodborne infective agents among people admitted to a Canadian hospital. Can. Med. Assoc. J. 146:1331–1334.
- 176. Mahoney, F. J., K. Stewart, H. Hu, P. Coleman, and M. Alter. 1997. Progress toward elimination of hepatitis B virus transmission among health care workers in the United States. Arch. Intern. Med. 157:2601–2605.
- 177. Mangione, C. M., J. L. Gerberding, and S. R. Cumings. 1991. Occupational exposure to HIV: frequency and rates of underreporting of percutaneous and mucocutaneous exposures by medical housestaff. Am. J. Med. 90:85– 90.
- 178. Marcus, R., D. H. Culver, D. M. Bell, P. U. Srivastava, M. H. Mendelson, R. J. Zalenski, B. Farber, D. Fligner, J. Hassett, T. C. Quinn, C. A. Schable, E. P. Sloan, P. Tsui, and G. D. Kelen. 1993. Risk of human immunodeficiency virus infection among emergency department workers. Am. J. Med. 94:363–369.
- 179. Reference deleted.
- Martin, M. A., M. Reichelderfer, and the Association for Professionals in Infection Control and Epidemiology, Inc. 1994. APIC guideline for infection prevention and control in flexible endoscopy. Am. J. Infect. Control 22:19–38.
- 181. Mast, E. E., and M. J. Alter. 1993. Prevention of hepatitis B virus infection among health-care workers, p. 295–307. *In R. W. Ellis (ed.)*, Hepatitis B vaccines in clinical practice. Marcel Dekker, Inc., New York, N.Y.

- Mast, S. T., J. D. Woolwine, and J. L. Gerberding. 1992. Efficacy of gloves in reducing blood volumes transferred during simulated needlestick injury. J. Infect. Dis. 168:1589–1592.
- McGeer, A., A. E. Simor, and D. E. Low. 1990. Epidemiology of needlestick injuries in house officers. J. Infect. Dis. 162:961–964.

- 185. Mishu, B., W. Schaffner, J. M. Horan, L. H. Wood, R. H. Hutcheson, and P. C. McNabb. 1990. A surgeon with AIDS: lack of evidence of transmission to patients. JAMA 264:467–470.
- 186. Mitsui, T., K. Iwano, K. Masuko, C. Yamazaki, H. Yakamoto, F. Tsuda, T. Tanaka, and S. Mishiro. 1992. Hepatitis C virus infection in medical personnel after needlestick accident. Hepatology 16:1109–1114.
- 187. Montecalvo, M. A., M. S. Lee, H. DePalma, P. S. Wynn, A. B. Lowenfels, U. Jorde, D. Wuest, A. Klingamen, T. A. O'Brien, M. Calmann, and G. P. Wormser. 1995. Seroprevalence of human immunodeficiency virus-1, hepatitis B virus, and hepatitis C virus in patients having major surgery. Infect. Control Hosp. Epidemiol. 16:627–632.
- Moyer, L. A., and M. J. Alter. 1994. Hepatitis C virus in the hemodialysis setting: a review with recommendations for control. Semin. Dialysis 7:124– 127.
- Moyer, L. A., M. J. Alter, and M. S. Favero. 1990. Hemodialysis-associated hepatitis B: revised recommendations for serologic screening. Semin. Dialysis 3:201–204.
- Mullins, J. R., and P. B. Harrison. 1993. The questionable utility of mandatory screening for the human immunodeficiency virus. Am. J. Surg. 166: 676–679.
- 191. Nagachinta, T., C. R. Gold, F. Cheng, P. N. R. Heseltine, and P. R. Kerndt. 1996. Unrecognized HIV-1 infection in inner-city emergency department patients. Infect. Control Hosp. Epidemiol. 17:174–177.
- 192. Nakano, Y., K. Kiyosawa, T. Sodeyama, E. Tanaka, A. Matsumoto, T. Ichijo, M. Mizokami, and S. Furuta. 1995. Acute hepatitis C transmitted by needlestick accident despite short duration interferon treatment. J. Gastro-enterol. Hepatol. 10:609–611.
- 193. Reference deleted.
- Natov, S. N., and B. J. Pereira. 1996. Hepatitis C in dialysis patients. Adv. Renal Replace. Ther. 3:275–283.
- Neal, K. R., J. Dornan, and W. L. Irving. 1997. Prevalence of hepatitis C antibodies among healthcare workers of two teaching hospitals: who is at risk? Br. Med. J. 314:179–180.
- 196. Neal, K. R., D. A. Jones, D. Killey, and V. James. 1994. Risk factors for hepatitis C virus infection: a case-control study of blood donors in the Trent Region (UK). Epidemiol. Infect. 112:595–601.
- 197. Niitsuma, H., M. Ishii, Y. Saito, M. Miura, K. Kobayashi, H. Ohori, and T. Toyota. 1995. Prevalence of precore-defective mutant of hepatitis B virus in HBV carriers. J. Med. Virol. 46:397–402.
- 198. Niu, M. T., L. T. Penberthy, M. J. Alter, C. W. Armstrong, G. B. Miller, and S. C. Hadler. 1989. Hemodialysis-associated hepatitis B: report of an outbreak. Dialysis Transplant. 18:542–545.
- 199. Niu, M. T., D. S. Stein, and S. M. Schnittmann. 1993. Primary human immunodeficiency virus type 1 infection: review of pathogenesis and early treatment interventions in humans and animal retrovirus infections. J. Infect. Dis. 168:1490–1501.
- 200. Noguchi, S., M. Sata, H. Suzuki, K. Ohba, M. Mizokami, and K. Tanikawa. 1997. Early therapy with interferon for acute hepatitis C acquired through a needlestick. Clin. Infect. Dis. 24:992–994.
- 201. Noone, P. A., I. S. Symington, and W. F. Carman. 1997. Hepatitis B and health care workers. Lancet 350:219.
- 201a.Noskin, G. A. 1995. Prevention, diagnosis, and management of viral hepatitis: a guide for primary care physicians. American Medical Association, Division of Health Science, Chicago, Ill.
- O'Briain, D. S. 1991. Patterns of occupational hand injury in pathology: the interaction of blades, needles, and the dissector's digits. Arch. Pathol. Lab. Med. 115:610–613.
- 203. Oguchi, H., M. Miyasaka, S. Tokunaga, K. Hora, S. Ichikawa, T. Ochi, K. Yamada, M. Nagasawa, Y. Kanno, T. Azizawa, et al. 1992. Hepatitis virus infection (HBV and HCV) in eleven Japanese hemodialysis units. Clin. Nephrol. 38:36–43.
- O'Neill, T. M., A. V. Abbott, and S. E. Radecki. 1992. Risk of needlesticks and occupational exposures among residents and medical students. Arch. Intern. Med. 152:1451–1456.
- Osborn, E. H. S., M. A. Papadakis, and J. L. Gerberding. 1999. Occupational exposures to body fluids among medical students: a seven-year longitudinal study. Ann. Intern. Med. 130:45–51.
- 206. Ou, C.-Y., C. A. Ciesielski, G. Myers, C. I. Bandea, C.-C. Luo, B. T. M. Korber, J. I. Mullins, G. Schochetman, R. L. Berkelman, A. N. Economou, J. J. Witte, L. J. Furman, G. A. Satten, K. A. MacInnes, J. W. Curran, H. W. Jaffe, Laboratory Investigation Group, and Epidemiologic Investigation Group. 1992. Molecular epidemiology of HIV transmission in a dental practice. Science 256:1165–1171.
- 207. Owens, D. K., M. Holodniy, A. M. Garber, J. Scott, S. Sonnad, L. Moses, B. Kinosian, and J. S. Schwartz. 1996. Polymerase chain reaction for the diagnosis of HIV infection in adults: a meta-analysis with recommendations

<sup>184.</sup> Reference deleted.

- 208. Panlilio, A. L., D. R. Foy, J. R. Edwards, D. M. Bell, B. A. Welch, C. M. Parrish, D. H. Culver, P. W. Lowry, W. R. Jarvis, and C. A. Perlino. 1991. Blood contacts during surgical procedures. JAMA 265:1533–1537.
- 209. Panlilio, A. L., C. N. Shapiro, C. A. Schable, M. H. Mendelson, M. A. Montecalvo, L. M. Kunches, S. W. Perry III, J. R. Edwards, P. U. Srivastava, D. H. Culver, I. B. Weisfuse, V. Jorde, J. M. Davis, J. Solomon, G. P. Wormser, J. Ryan, D. M. Bell, M. E. Chamberland, and the Serosurvey Study Group. 1995. Serosurvey of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus infection among hospital-based surgeons. J. Am. Coll. Surg. 180:16–24.
- 210. Panlilio, A. L., B. A. Welch, D. M. Bell, D. R. Foy, C. M. Parrish, C. A. Perlino, and L. Klein. 1992. Blood and amniotic fluid contact sustained by obstetric personnel during deliveries. Am. J. Obstet. Gynecol. 167:703–708.
- Pattison, C. P., K. M. Boyer, J. E. Maynard, and P. C. Kelly. 1974. Epidemic hepatitis in a clinical laboratory: possible association with computer card handling. JAMA 230:854–857.
- Pawlotsky, J.-M. 1997. Measuring hepatitis C viremia in clinical samples: can we trust the assays? Hepatology 26:1–4.
- Pereira, B. J., and A. S. Levey. 1997. Hepatitis C virus infection in dialysis and renal transplantation. Kidney Int. 51:981–999.
- 214. Reference deleted.
- Peterman, T. A., G. R. Lang, N. J. Mikos, S. L. Solomon, C. A. Schable, P. M. Feorino, J. A. Britz, and J. R. Allen. 1986. HTLV-III/LAV infection in hemodialysis patients. JAMA 255:2324–2326.
- Peters, M., G. L. Davis, J. S. Dooley, and J. H. Hoofnagle. 1986. The interferon system in acute and chronic viral hepatitis. Prog. Liver Dis. 8:453–467.
- Polakoff, S. 1986. Acute hepatitis B in patients in Britain related to previous operations and dental treatment. Br. Med. J. Clin. Res. 293:33–36.
- Polakoff, S. 1986. Acute viral hepatitis B: laboratory reports 1980–4. Br. Med. J. Clin. Res. 293:37–38.
- Polish, L. B., M. J. Tong, R. L. Co, P. J. Coleman, and M. J. Alter. 1993. Risk factors for hepatitis C virus infection among healthcare personnel in a community hospital. Am. J. Infect. Control 21:196–200.
- Popejoy, S. L., and D. E. Fry. 1991. Blood contact and exposure in the operating room. Surg. Gynecol. Obstet. 172:480–483.
- Prentice, M. B. 1992. Infection with hepatitis B virus after open heart surgery. Br. Med. J. 304:761–764.
- Prince, A. M. 1994. Challenges for development of hepatitis C virus vaccines. FEMS Microbiol. Rev. 14:273–277.
- Puro, V., N. Petrosillo, and G. Ippolito. 1995. Risk of hepatitis C seroconversion after occupational exposures in health care workers. Am. J. Infect. Control 23:273–277.
- 224. Quebbeman, E. J., G. L. Telford, S. Hubbard, K. Wadsworth, B. Hardman, H. Goodman, and M. S. Gottlieb. 1991. Risk of blood contamination and injury to operating room personnel. Ann. Surg. 214:614–620.
- 225. Ranki, A., S. Mattinen, R. Yarchoan, S. Broder, J. Ghrayeb, J. Lehdevirta, and K. Krohn. 1989. T-cell response towards HIV in infected individuals with and without zidovudine therapy, and in HIV-exposed sexual partners. AIDS 3:63–69.
- 226. Ridzon, R., K. Gallagher, C. Ciesielski, M. B. Ginsberg, B. J. Robertson, C.-C. Luo, and A. DeMana, Jr. 1997. Simultaneous transmission of human immunodeficiency virus and hepatitis C virus from a needle-stick injury. N. Engl. J. Med. 336:919–922.
- 227. Robert, L. M., M. E. Chamberland, J. L. Cleveland, R. Marcus, B. F. Gooch, P. U. Srivastava, D. H. Culver, H. W. Jaffe, D. W. Marianos, A. L. Panlilio, and D. M. Bell. 1995. Investigations of patients of health care workers infected with HIV: the Centers for Disease Control and Prevention database. Ann. Intern. Med. 122:653–657.
- Rogers, A. S., J. W. Froggatt III, T. Townsend, T. Gordon, A. J. L. Brown, E. C. Holmes, L. A. Zhang, and H. Moses III. 1993. Investigation of potential HIV transmission to the patients of an HIV-infected surgeon. JAMA 269:1795–1801.
- Roth, W. K., J.-H. Lee, B. Ruster, and S. Zeuzem. 1996. Comparison of two quantitative hepatitis C virus reverse transcriptase PCR assays. J. Clin. Microbiol. 34:261–264.
- Ruprecht, R. M., L. G. O'Brien, L. D. Rossoni, and S. Nusinoff-Lehrman. 1986. Suppression of mouse viraemia and retroviral disease by 3'-azido-3'deoxythymidine. Nature 323:467–469.
- 231. Sanchez-Quijano, A., J. A. Pineda, E. Lissen, M. Leal, M. A. Diaz-Torres, F. Garcia de Pesquera, F. Rivera, R. Castro, and J. Munoz. 1988. Prevention of post-transfusion non-A, non-B hepatitis by non-specific immunoglobulin in heart surgery patients. Lancet i:1245–1249.
- 232. Satori, M., G. La Terra, M. Aglietta, A. Manzin, C. Navino, and G. Verzetti. 1993. Transmission of hepatitis C via blood splash into conjunctiva. Scand. J. Infect. Dis. 25:270–271.
- Sattar, S. A., and V. S. Springthorpe. 1991. Survival and disinfectant inactivation of the human immunodeficiency virus. Rev. Infect. Dis. 13:430–447.
- Schlipkoter, U., M. Roggendorf, K. Cholmakow, A. Weise, and F. Deinhardt. 1990. Transmission of hepatitis C virus (HCV) from a haemodialysis

patient to a medical staff member. Scand. J. Infect. Dis. 22:757-758.

- 235. Reference deleted.
- 236. Schneiderman, L. J., and R. M. Kaplan. 1992. Fear of dying and HIV infection vs hepatitis B infection. Am. J. Infect. Control 82:584–586.
- 237. Reference deleted.
- 238. Seeff, L. B., H. J. Zimmerman, E. C. Wright, J. D. Finkelstein, P. Garcia-Pont, H. B. Greenlee, A. A. Dietz, C. M. Leevy, C. H. Tamburro, E. R. Schiff, R. Zemel, D. S. Zimmon, and R. W. McCollom. 1977. A randomized, double blind controlled trial of the efficacy of immune serum globulin for the prevention of post-transfusion hepatitis: a Veterans Administration cooperative study. Gastroenterology 72:111–121.
- 239. Segal, H. E., C. H. Llewellyn, G. Irwin, W. H. Bancroft, G. P. Boe, and D. J. Balaban. 1976. Hepatitis B antigen and antibody in the US Army: prevalence in health care personnel. Am. J. Public Health 66:667–671.
- 240. Selgas, R., R. Martinez-Zapico, M. A. Bajo, J. R. Romero, J. Munoz, C. Rinon, B. Miranda, and J. L. Miguel. 1992. Prevalence of hepatitis C antibodies (HCV) in a dialysis population at one center. Perit. Dial. Int. 12:28–30.
- 241. Shapiro, C. N., J. I. Tokars, and M. E. Chamberland. 1996. Use of the hepatitis B vaccine and infection with hepatitis B and C among orthopaedic surgeons. J. Bone Joint Surg. 78:1791–1800.
- 242. Shih, C.-C., H. Kaneshima, L. Rabin, R. Namikawa, P. Sager, J. McGowan, and J. M. McCune. 1991. Postexposure prophylaxis with zidovudine suppressed human immunodeficiency virus type 1 infection in SCID-hu mice in a time-dependent manner. J. Infect. Dis. 163:625–627.
- 243. Shikata, T., T. Karasawa, K. Abe, T. Uzawa, H. Suzuki, T. Oda, M. Imai, M. Mayumi, and Y. Moritsugu. 1977. Hepatitis B antigen and infectivity of hepatitis B virus. J. Infect. Dis. 136:571–576.
- 244. Reference deleted.
- 245. Reference deleted.
- 246. Smith, J. L., J. E. Maynard, K. R. Berquist, I. L. Doto, H. M. Webster, and M. J. Sheller. 1976. Comparative risk of hepatitis B among physicians and dentists. J. Infect. Dis. 133:705–706.
- 247. Sodeyama, T., K. Kiyosawa, and A. Urushihara. 1993. Detection of hepatitis C virus markers and hepatitis C virus genomic-RNA after needlestick accidents. Arch. Intern. Med. 153:1565–1572.
- 248. Sperling, R. S., D. E. Shapiro, R. W. Coombs, J. A. Todd, S. A. Herman, G. D. McSherry, M. J. O'Sullivan, R. B. VanDyke, E. Jiminez, C. Rouzioux, P. M. Flynn, and J. L. Sullivan. 1996. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. N. Engl. J. Med. 335:1621–1629.
- 249. Struve, J., B. Aronsson, B. Frenning, M. Forsgren, and O. Weiland. 1994. Prevalence of antibodies against hepatitis C virus infection among healthcare workers in Stockholm. Scand. J. Gastroenterol. 29:360–362.
- 250. Sundkvist, T., G. R. Hamilton, D. Rimmer, B. G. Evans, and C. G. Teo. 1998. Fatal outcome of transmission of hepatitis B from an e antigen negative surgeon. Commun. Dis. Public Health 1:48–50.
- 251. Tavares, L., C. Roneker, K. Johnston, S. N. Lehrman, and F. de Noronha. 1987. 3'-Azido-3'-deoxythymidine in feline leukemia virus-infected cats: a model for therapy and prophylaxis of AIDS. Cancer Res. 47:3190–3194.
- Terrell, F., and B. Williams. 1993. Implementation of a customized needleless intravenous delivery system. J. Intraven. Nurs. 16:339–344.
- 253. Thomas, D. L., S. E. Gruninger, C. Siew, E. D. Joy, and T. C. Quinn. 1996. Occupational risk of hepatitis C infections among general dentists and oral surgeons in North America. Am. J. Med. 100:41–45.
- 254. Tokars, J. I., M. J. Alter, and M. S. Favero. 1995. National surveillance of dialysis-associated diseases in the United States, 1993. Centers for Disease Control and Prevention, Atlanta, Ga.
- 255. Tokars, J. I., M. J. Alter, M. S. Favero, L. A. Moyer, E. Miller, and L. A. Bland. 1994. National surveillance of dialysis associated diseases in the United States, 1992. ASAIO J. 40:1020–1031.
- 256. Tokars, J. I., D. M. Bell, D. H. Culver, R. Marcus, M. H. Mendelson, E. P. Sloan, B. F. Farber, D. Fligner, M. E. Chamberland, P. S. McKibben, and W. J. Martone. 1992. Percutaneous injuries during surgical procedures. JAMA 267:2899–2904.
- 257. Reference deleted.
- 258. Tokars, J. I., M. E. Chamberland, C. A. Schable, D. H. Culver, M. Jones, P. S. McKibben, D. M. Bell, and the American Academy of Orthopaedic Surgeons Serosurvey Study Committee. 1992. A survey of occupational blood contact and HIV infection among orthopedic surgeons. JAMA 268: 489–494.
- 259. Tokars, J. I., D. H. Culver, M. H. Mendelson, E. P. Sloan, B. F. Farber, D. J. Fligner, M. E. Chamberland, R. Marcus, P. S. McKibben, and D. M. Bell. 1995. Skin and mucous membrane contacts with blood during surgical procedures: risk and prevention. Infect. Control Hosp. Epidemiol. 16:703– 711.
- 260. Tong, S., and C. Trepo. 1997. The HBe-minus mutants of hepatitis B virus, p. 89–104. *In* T. J. Harrison and A. J. Zuckerman (ed.), The molecular medicine of viral hepatitis. John Wiley and Sons, Ltd., Chichester, United Kingdom.
- 261. Trepka, M. J., A. J. Davidson, and J. M. Douglas, Jr. 1996. Extent of undiagnosed HIV infection in hospitalized patients: assessment by linkage

of seroprevalence and surveillance methods. Am. J. Prev. Med. 12:195-202.

- 262. Tsai, C.-C., K. E. Follis, A. Sabo, T. W. Beck, R. F. Grant, N. Bischofberger, R. E. Benveniste, and R. Black. 1995. Prevention of SIV infection in macaques by (*R*)-9-(2-phosphonylmethoxyprophyl) adenosine. Nature 270:1197–1199.
- 263. Tsude, K., S. Fujiyama, S. Sato, S. Kawano, Y. Taura, K. Yoshida, and T. Sato. 1992. Two cases of accidental transmission of hepatitis C to medical staff. Hepatogastroenterology 39:73–75.
- 264. Turner, S. B., L. M. Kunches, K. F. Gordon, P. H. Travers, and N. E. Mueller. 1989. Occupational exposure to human immunodeficiency virus (HIV) and hepatitis B virus (HBV) among embalmers: a pilot seroprevalence study. Am. J. Public Health 79:1425–1426.
- 265. Reference deleted.
- 266. U.S. Department of Labor Occupation Safety and Health Administration. 1991. 29 CFR Part 1910.1030, Occupational exposure to bloodborne pathogens: final rule. Fed. Regist. 56:64004–64182.
- 266a. U.S. Food and Drug Administration. 1997. Protease inhibitors may increase blood glucose in HIV patients. FDA Medical Bulletin 27.
- Van Bueren, J., R. A. Simpson, P. Jacobs, and B. D. Cookson. 1994. Survival of human immunodeficiency virus in suspension and dried onto surfaces. J. Clin. Microbiol. 32:571–574.
- Vaqlia, A., R. Nicolin, V. Puro, G. Ippolito, C. Bettini, and F. de Lalla. 1990. Needlestick hepatitis C virus seroconversion in a surgeon. Lancet 336:1315– 1316.
- Villarejos, V. M., K. A. Visona, and A. Guitierrez. 1974. Role of saliva, urine and feces in the transmission of type B hepatitis. N. Engl. J. Med. 291: 1374–1378.
- 270. Vogel, W., I. Graziadei, F. Umlauft, C. Datz, F. Hackl, S. Allinger, K. Grunewald, and J. Patsch. 1996. High-dose interferon-alpha2b treatment prevents chronicity in acute hepatitis C: a pilot study. Dig. Dis. Sci. 41(Suppl. 12):81S–85S.
- 271. von Reyn, C. F., T. T. Gilbert, F. E. Shaw, K. C. Parsonnet, J. E. Abramson, and M. G. Smith. 1993. Absence of HIV transmission from an infected orthopedic surgeon: a 13-year look-back study. JAMA 269:1807–1811.
- 272. Wainwright, R. B., B. J. McMahon, L. R. Bulkow, D. B. Hall, M. A.

Fitzgerald, A. P. Harpster, S. C. Hadler, A. P. Lanier, and W. L. Heyward. 1989. Duration of immunogenicity and efficacy of hepatitis B vaccine in a Yupik Eskimo population. JAMA 261:2362–2366.

- 273. Reference deleted.
- 274. Reference deleted.
- 275. Welch, J., M. Webster, A. J. Tilzey, N. D. Noah, and J. E. Banatvala. 1989. Hepatitis B infections after gynaecological surgery. Lancet i:205–207.
- Werman, H. A., and R. Gwinn. 1997. Seroprevalence of hepatitis B and hepatitis C among rural emergency medical care personnel. Am. J. Emerg. Med. 15:248–251.
- 277. Werner, B. G., and G. F. Grady. 1982. Accidental hepatitis B surface antigen positive inoculations: use of e antigen to estimate infectivity. Ann. Intern. Med. 97:367–369.
- West, D. J. 1984. The risk of hepatitis B infection among health professionals in the United States: a review. Am. J. Med. Sci. 287:26–33.
- 279. West, D. J., B. Watson, J. Lichtman, T. M. Hesley, and K. Hedberg. 1994. Persistence of immunologic memory for twelve years in children given hepatitis B vaccine in infancy. Pediatr. Infect. Dis. J. 13:745–747.
- Whittle, H. C., N. Maine, J. Pilkington, M. Mendy, M. Fortuin, J. Bunn, L. Allison, C. Howard, and A. Hall. 1995. Long-term efficacy of continuing hepatitis B vaccination in infancy in two Gambian villages. Lancet 345: 1089–1092.
- Willy, M. E., G. L. Dhillon, N. L. Loewen, R. A. Wesley, and D. K. Henderson. 1990. Adverse exposures and universal precautions practices among a group of highly exposed health professionals. Infect. Control Hosp. Epidemiol. 11:351–356.
- 282. Wong, E. S., J. L. Stotka, V. M. Chinchilli, D. S. Williams, C. G. Stuart, and S. M. Markowitz. 1991. Are universal precautions effective in reducing the number of occupational exposures among health care workers? A prospective study of physicians on a medical service. JAMA 265:1123–1128.
- 283. Younossi, Z., and J. McHutchison. 1996. Serologic tests for HCV infection. Viral Hepatitis Rev. 2:161–173.
- Zuckerman, J., G. Clewley, P. Griffiths, and A. Cockcroft. 1994. Prevalence of hepatitis C antibodies in clinical health-care workers. Lancet 343:1618– 1620.