

Blood-borne pathogens and nosocomial infections

Donald A. Goldman, MD *Boston, Mass*

Guidelines to prevent the transmission of blood-borne infections have evolved rapidly since the recognition that "serum hepatitis" could be transmitted to health care personnel via percutaneous exposure to blood. The HIV epidemic focused renewed attention on the problem of protecting health care personnel, culminating in "standard precautions" for patient care, which emphasized the use of gloves for all contact with blood and body fluids. This focus on protection of the health care worker sometimes obscures the other important functions of gloves: protection of patients from microorganisms on the hands of providers and prevention of patient-to-patient transmission of nosocomial pathogens. The risk of infection after percutaneous exposure to the 3 major blood-borne viruses— hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV— varies greatly. The risk for a nonimmune individual exposed to HBV may be >30% if the source is Hb_eAg-positive. The average infection rate for HCV is 1.8%. For HIV, the average risk is 0.3%, but is higher with deep injury, when there is visible blood on the device, when a needle has been in an artery or vein, or when the source patient is in the terminal phase of HIV. Prompt administration of anti-HIV therapy reduces risk by about 80%. Mucous membrane and cutaneous exposures carry less risk. Recent efforts to reduce needlestick injuries in hospitals have reduced the risk to health care providers. Surgeons and other health care professionals who are infected with HIV or HCV pose a very small risk to their patients, although a number of outbreaks have been traced to surgeons who are HBV carriers; most have been Hb_eAg-positive. (*J Allergy Clin Immunol* 2002;110:S21-6.)

Key words: Blood-borne infection, nosocomial infection, occupational health, hepatitis B virus, hepatitis C virus, HIV

INFECTION CONTROL CONTEXT

Even before the birth of the germ theory, the courageous people who cared for the sick tried as hard as they could to protect themselves from contagion. In the late Middle Ages, for example, the brave souls who volunteered to care for victims of the plague wore masks designed to shield them from the vapors (or miasmas)

Abbreviations used

BSE: Bovine spongiform encephalopathy
BSI: Body substance isolation
CDC: Centers for Disease Control and Prevention
CJD: Creutzfeldt-Jakob disease
HBV: Hepatitis B virus
HCV: Hepatitis C virus

that they thought transmitted this lethal illness. Modern concepts of disease transmission are more sophisticated, and personal protective gear has evolved accordingly. In the industrialized world, high-performance gloves, water-impermeable gowns, highly efficient masks, and impervious face shields are all part of the contemporary health care worker's standard gear. Of course, health care providers in developing countries are not always so fortunate. The brave nurses and doctors who care for patients with hemorrhagic fevers, such as Lassa fever and Ebola virus, have experienced extraordinarily high fatality rates. Retrospective epidemiologic analysis of these outbreaks has invariably shown that health care providers did not have access to the gloves, gowns, and masks that almost assuredly would have protected them from infection and death. Moreover, even when such equipment was available, training in its use was inadequate.

Health care providers often seem confused about the purpose of the protective gear they wear. Fear of blood-borne diseases tends to be the prime motivator for hospital personnel. When the first patients with AIDS were admitted to hospital wards in the United States, staff often donned protective garb for even the most casual contact with infected patients. Understanding of the modes of transmission of HIV quickly led to an appropriate relaxation of behavior. The same members of the ward team who had put on gloves and gowns just to examine the chest of a hospitalized AIDS patient in the first year of the outbreak did not even bother to wash their hands after examining a similar patient a year later. Nonetheless, fear of exposure to AIDS and other blood-borne viral infections is still the prime incentive for personnel to wear gloves, gowns, and other protective equipment during patient care. It is sometimes forgotten that these shields have other important functions in patient care, apart from protecting the staff from contagious diseases. Gloves protect patients from microorganisms during surgical procedures and the insertion of invasive devices, such as central venous catheters. In addition, gloves may reduce the small risk to patients from caregivers who are carriers of a blood-borne virus, an issue that is discussed in greater detail below.

From the Department of Medicine and Infection Control Program, Children's Hospital, and the Department of Pediatrics, Harvard Medical School, Boston.

Dr Goldman has no significant financial interest in the commercial sponsors of this publication. He attests that there is no commercial or personal conflict of interest.

Reprint requests: Donald A. Goldman, MD, Division of Infectious Diseases, 300 Longwood Ave, Boston, MA 02115; E-mail: Don.Goldman@tch.harvard.edu.

© 2002 Mosby, Inc. All rights reserved.
0091-6749/2002/\$35.00 + 0 1/0/125337
doi:10.1067/mai.2002.125337

Gloves play a particularly important role in preventing nosocomial patient-to-patient transmission of bacteria, viruses, and fungi via contaminated hands of caregivers. Indeed, gloves, supplemented by appropriate hand hygiene, are at the very core of all efforts to control the spread of nosocomial pathogens, including antimicrobial-resistant bacteria. Hospitalized patients, especially critically ill patients who require intensive care, tend to be colonized with the nosocomial pathogens that are prevalent on the wards to which they are admitted. Typically, they excrete very high concentrations of these pathogens in their stool and respiratory secretions, often reaching 10^9 bacteria per gram of stool or per milliliter of sputum. Even a speck of these heavily contaminated materials can contaminate the hands with a large number of microorganisms, unless the provider wears gloves and washes his or her hands. Personnel who fail to adhere to these basic infection control techniques place patients under their care at grave risk for colonization and infection.

Confusion regarding the role of gloves for personal *versus* patient protection occasionally leads to bizarre behavior. Take the caregiver who wears the same pair of gloves as he moves from patient to patient, oblivious to the fact that many nosocomial pathogens survive quite well on the surface of gloves, just as they do on the ungloved hand, or the physician who removes her gloves appropriately when leaving the bedside but fails to wash her hands, despite convincing evidence that hands are easily contaminated during glove removal.¹

A brief review of the recent history of barrier precautions in hospitals is useful in elucidating how the attitudes and beliefs of infection control experts regarding gloves, gowns, and other protective equipment have evolved over time. The numerous changes in national recommendations have less to do with new scientific evidence than with the difficulty of blending the various purposes of barriers into a single coherent policy.

The Centers for Disease Control and Prevention (CDC) first published isolation recommendations in 1970.² Seven categories of isolation were described, based on the general modes of transmission of nosocomial pathogens. Because it had clearly been established, as early as 1949, that health care workers could contract blood-borne hepatitis ("serum hepatitis") from patients,³⁻⁶ "blood precautions" was one of these categories. Subsequently, the CDC streamlined these category-specific precautions (including changing the term *blood-borne precautions* to *blood and body fluid precautions*) and added recommendations for the isolation of specific diseases. These guidelines, which were published in 1983, proved confusing, largely because hospital infection control programs were asked to choose between category-specific and diseases-specific isolation systems.⁷ Interpretation of the guidelines also required front-line hospital staff to understand how specific pathogens are transmitted, an expectation that remains unrealized to this day. Most importantly for the present discussion, the AIDS epidemic quickly rendered the concept of blood and body fluid precautions obsolete. It was recognized that many patients harbor

HIV (and other blood-borne pathogens) and are potentially infectious to health care providers even though they have not yet been given the diagnosis. Therefore, health care workers were instructed to regard the blood of *all* patients as potentially infectious and to protect themselves routinely when exposure to blood or body secretions containing blood was expected. In 1985, the CDC issued formal recommendations for such "universal precautions."⁸ By 1987,⁹ universal precautions had been codified to include blood, semen, vaginal secretions, and various body fluids (amniotic, cerebrospinal, pericardial, peritoneal, pleural, and synovial fluids), as well as any fluid visibly contaminated with blood. One of the unintended sequelae of these guidelines was an acute shortage of latex gloves. As manufacturers struggled to meet the demand, products of variable quality appeared in the marketplace, and it was years before supply of uniformly high-quality gloves caught up with demand.

Just as infection control professionals were beginning to apply these new standards, a novel guideline system called *Body Substance Isolation* (BSI) was published by workers in Seattle and San Diego.¹⁰ BSI applied to all patients and required gloves for contact with moist substances, mucous membranes, and nonintact skin. BSI had intuitive appeal because it required little training or knowledge, incorporated the principles of universal precautions for protection of personnel, and was based on the assumption that all "body substances" were potentially contaminated and could serve as a source for patient-to-patient transmission of microorganisms. Weaknesses of the system included sketchy provisions for diseases spread by droplets, through the air, or via environmental contamination. BSI was also expensive to implement because it increased glove use. Moreover, the need to wash hands after removal of gloves was not emphasized. Meanwhile, in 1989 and 1991, the Occupational Safety and Health Administration issued stringent rules regarding occupational exposure to blood-borne pathogens, based largely on the concepts of universal precautions.^{11,12}

Confusion and inconsistency reigned, leading to yet another CDC isolation guideline in 1996.¹³ This guideline incorporated the basic tenets of BSI and universal precautions in "standard precautions" for all patients. Standard precautions apply to blood, all body fluids and secretions except sweat (regardless of whether they contain visible blood), nonintact skin, and mucous membranes. In addition, 3 categories of isolation were designated based on the major modes of microbial transmission—airborne, droplet, and contact. Special attention was given to certain epidemiologically important antimicrobial-resistant pathogens. These guidelines were a distinct improvement but still required local modification and refinement, especially in pediatrics. They left infection control staff with the obligation to emphasize that gloves are required to protect both the hospital worker *and* the patient.

Individual blood-borne pathogens have specific risks and consequences, and it is important to differentiate among them. Each of the 3 principal blood-borne pathogens is discussed briefly: hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV.

RISK TO HEALTHCARE WORKERS

HBV was the pathogen that first alerted the medical community to the occupational dangers of blood-borne viruses. The problem was especially grave before introduction of appropriate procedures to protect personnel from exposure to blood and before introduction of safe, effective hepatitis vaccines. At that time, the risk of HBV was much higher for health care workers than for the general population—more than 10-fold higher for certain high-risk groups such as surgeons, dialysis workers, and dentists.¹⁴⁻¹⁶ In 1983, the incidence of HBV infection in health care workers was 386 per 100,000.¹⁴ Because approximately 10% of acutely infected individuals become chronic carriers of the virus and are at risk for cirrhosis and hepatocellular carcinoma, the morbidity and mortality rates associated with occupationally acquired disease were substantial. Fortunately, the incidence of infection has declined steadily over the years to 9.1 per 100,000 in 1995,¹⁴ and health care workers now appear to be at an even lower risk than the general population.

Immunization of health care workers is especially important because the risk of contracting disease from a single percutaneous exposure to HBV-infected blood is very high, ranging from 6% to more than 30% in various studies.¹⁷⁻²⁰ The highest risk is associated with exposure to Hb_eAg-positive blood, which can contain 10⁹ virions per milliliter.¹⁷ Thus, a needlestick injury with a 22-gauge needle may expose the victim to 100 infectious doses of virus. Titers of virus in saliva are much lower than in blood (although saliva is considered potentially infectious), and titers in other body fluids, such as urine and feces, are very low or undetectable. Personnel who are exposed to blood or other infectious materials by means of splashes to mucous membranes or because they have cuts or abrasions on their skin are considered at risk, although the precise magnitude of the risk is unclear.

HCV is considered a silent, deadly epidemic because the majority of infected patients do not yet know they are carrying the virus. In the 1980s, an estimated 230,000 new infections occurred annually in the United States.²¹ Although the annual number of new infections declined to about 36,000 in 1996,²²⁻²⁴ as many as 3.9 million Americans have been infected with HCV. The rate of chronic infection (which often is asymptomatic for long periods) is extraordinarily high—probably at least 85%. Chronic liver disease may develop in up to 70% of infected patients, resulting in 8000 to 10,000 deaths per year and an economic burden of >\$600 million annually.

These are fearsome statistics, but are health care workers at substantially increased risk for HCV? Certainly, health care personnel do not fall among the major risk groups, which include drug users; patients undergoing hemodialysis on a long-term basis; persons who were treated for hemophilia or received blood transfusions in the 1980s or earlier; and people with multiple sex partners, sexually transmitted diseases, and HIV. In fact, aggregate serologic data suggest that health care workers (including general, orthopedic, and oral surgeons) have a

prevalence of HCV infection similar to that of the general population.²² Nonetheless, HCV can clearly be transmitted by percutaneous exposure to contaminated blood in health care settings. The risk from a single percutaneous exposure appears to be about 1.8% (range, 0%-7%),^{21,25} and a history of an accidental needle exposure is independently associated with anti-HCV positivity.²⁶ One study suggested that transmission occurs principally, even exclusively, through hollow-bore needles.²⁷ The lower rate of transmission compared with HBV probably reflects much lower blood titers of virus.^{28,29} The potential importance of mucous membrane and cutaneous exposure to health care personnel has not been determined, but the risk is probably very low. There have been very few case reports of transmission of HCV from blood splashes to the conjunctiva.^{30,31} Unfortunately, unlike HBV, there is no vaccine for HCV, and postexposure treatment with immune globulin is ineffective.²²

Recent studies have provided major insights into the epidemiology of HIV transmission in the workplace.^{32,33} The CDC had documented 56 cases of occupationally acquired HIV infection as of June 1999 (E. Beltrami, CDC, oral communication, 2001). The majority of cases were in clinical laboratory technicians and nurses. The average risk of transmission after percutaneous exposure to contaminated blood is approximately 0.3%, but the risk varies greatly according to the specific circumstances. For example, the risk of HIV is increased 15-fold with a deep injury, 6.2-fold when there is visible blood on the device, 4.3-fold in procedures involving a needle placed in an artery or vein, and 5.6-fold when the source patient is in the terminal phase of AIDS.³³ These data suggest that the titer of virus in the blood of the source patient is a critical factor in transmission. Presumably, hollow-bore needles pose a greater risk than solid suture needles because the volume of inoculated blood is greater. Mucus membrane exposures are less hazardous (0.1% risk). No health care worker enrolled in a prospective study has acquired HIV through contact of blood with nonintact skin, so the risk appears to be small.³² There is no evidence for transmission via aerosols of blood, even during orthopedic procedures in which such aerosols are commonplace.³⁴ The good news from the epidemiologic studies that defined the risk of exposure to HIV-contaminated blood is that postexposure prophylaxis, if administered promptly, reduces risk by about 5-fold.³³

RISK TO PATIENTS

The other side of the coin, the risk that health care providers will transmit blood-borne infections to their patients, provokes even more passion and debate than policies designed to ensure the safety of the workers. It has been known for years that infected providers can transmit HBV to patients. There have been more than 45 reports of HBV transmission to patients during invasive procedures, mostly in years before public awareness of the potential problem.³⁵ Almost all of the implicated health care workers were positive for Hb_eAg, as would be expected, given

their very high bloodstream viral titers in comparison with infected, but Hb_eAg-negative, individuals. However, transmission by Hb_eAg-negative surgeons has been reported in Great Britain. These individuals carried a precore mutant in the hepatitis genome that interrupts expression of the e antigen.¹⁷ Some surgeon-to-patient hepatitis clusters have been traced to obvious breaks in sound surgical technique or infection control practice.¹⁷ The cause of other outbreaks has been harder to decipher. For example, 13% of the 142 patients operated on by a cardiothoracic surgeon were infected, even though no problems with his surgical infection control practices had been documented.³⁶ In a surgery simulation experiment, the surgeon tied knots for 1 hour, skin breaks were observed on his fingers, and hepatitis B surface antigen (Hb_sAg) was detected when his gloves were rinsed with saline solution.

There have been only a few reports of provider-to-patient transmission of HCV.^{37,38} In an interesting recent outbreak, molecular epidemiologic methods were used to trace transmission of HCV from a patient to an anesthesiology assistant, with subsequent transmission to 5 of the assistant's patients.³⁹ The assistant seldom wore gloves because he felt that they impaired his sense of touch. At the time of the outbreak, he had a weeping wound on his finger, suggesting that he might have acquired hepatitis from the index patient through cutaneous exposure. The mechanism by which he subsequently transmitted virus to the other 5 patients is unclear but could have been due to contact between his wound and the patients' mucous membranes.

The potential danger that infected health care workers pose for their patients was brought into sharp national focus when molecular genetic testing implicated an HIV-infected dentist in Florida as the source of HIV infection in 6 patients.⁴⁰ The precise way in which this dentist might have infected his patients was never determined, but the episode led to a near-panic public reaction and rapid development of policies designed to limit the exposure of patients to HIV-positive providers. A second case, reported in 1997, was accompanied by renewed public anxiety.³² A French surgeon had performed operations on 3994 individuals over a number of years while HIV-positive; one of his patients was found to be infected with an identical HIV strain. The patient had undergone a 10-hour procedure at a time that the surgeon presumably had a high titer of circulating HIV. Despite these two episodes, the majority of evidence suggests that the likelihood of provider-to-patient transmission of HIV is extraordinarily small. Six retrospective investigations of patients of infected surgeons and dentists revealed no patients with HIV who could be positively linked to the practitioners and had no other risk factors.⁴¹⁻⁴⁶ A total of 4752 patients were tested for HIV in these studies. In addition, a CDC survey of all published and unpublished studies through January 1995 (22,171 patients) revealed only 15 HIV-positive individuals who did not have clearly established risk factors but had opportunities for exposure, plus 5 patients who had no definable risk factors.⁴⁷ Genetic typing of strains from 3 of the 5 patients with no risk factors and 13 of 15 patients with opportunities for exposure demonstrated no concordance

between patient and health care worker HIV strains. These results suggest the need to recalibrate current concerns regarding the danger infected providers pose to patients.

PERSONAL PROTECTION

Health care professionals who follow standard precautions to the letter certainly can reduce their risk of exposure to blood-borne viruses.⁴⁷⁻⁵⁰ However, high-quality gloves, impermeable gowns, and face shields do not address the entire problem. Gloves generally do not prevent needle punctures (although they may reduce the volume of blood that reaches the skin). If needles are improperly handled or disposed of carelessly, the primary provider places his or her colleagues, including environmental services personnel, at risk. Although it used to be common practice to leave needles lying around patient care areas, virtually all health care institutions now have appropriate puncture-proof needle disposal systems. However, these systems still require timely emptying or disposal. A variety of blood drawing practices can reduce the risk of needle puncture, such as consolidating blood draws and using needleless ports to obtain blood samples.³² The common practice of changing needles when culturing blood does not reduce the risk of blood culture contamination but does increase the risk of injury. So-called engineering interventions designed to make intravenous systems and venipuncture devices safer have had a profound impact on the risk of needlesticks on the wards, and a variety of protected or needleless devices are now commercially available.⁵¹⁻⁵³ Legislation to ensure adoption of safer systems has recently been passed.

Injury prevention during surgical procedures is more challenging. A number of epidemiologic studies have demonstrated that percutaneous exposures are more likely to occur in the operating room during lengthy procedures; when blood loss exceeds 250 to 300 mL; and during selected major procedures, such as intraabdominal gynecologic procedures, vaginal hysterectomies, major vascular procedures, and orthopedic surgeries.⁵⁴⁻⁶² Blunted suturing needles appear to be a major technological advance because they reduce the risk of injury substantially.³² Chiarello and Gerberding³² have made sensible recommendations for reducing sharps injuries in the operating room. These include using instruments instead of hands to retract and explore tissue, avoiding simultaneous presence of the hands of two surgeons in the surgical field, announcing when sharps need to be passed, and avoiding direct person-to-person passing of sharps.

Gloves are the principal barrier between surgeon and patient, protecting both parties. Glove perforation or loss of integrity during surgery is surprisingly common.⁶³⁻⁶⁹ Although surgeons may resist donning 2 pairs of gloves because of technical concerns, there is no doubt that double gloving is effective in reducing the risk of inner glove puncture.⁶⁹⁻⁷⁸ There is little evidence to indicate that double gloving has a significant impact on surgical dexterity or performance. Chiarello and Gerberding³² have noted that because most punctures occur on the

thumb, index, and middle fingers, reinforcing gloves in these areas is logical. Novel glove materials with improved resistance to punctures would be welcome.

Data from the CDC's National Surveillance System for Hospital Healthcare Workers clearly delineate the epidemiology of exposure to blood and other potentially infectious materials in the workplace and the magnitude of the risk workers continue to face. Complete data are available on the National Surveillance System for Hospital Healthcare Workers Web site (www.cdc.gov/ncidod/hip/NASH/report99.PDF). Most exposures occur in inpatient wards (30%), operating or procedure rooms (29%), intensive care units (13%), and emergency and outpatient departments (15% combined). Rates of exposure in central processing areas and laboratories are lower but still important. Not surprisingly, nurses (44%) and physicians (30%) are at highest risk. Syringe needles (34%), suture needles (16%), butterfly needles (13%), and scalpels (7%) are the most frequent causes of percutaneous injuries. Percutaneous exposures to hollow-bore needles (which tend to pose the highest risk) occur most often during phlebotomy (25%), intramuscular or subcutaneous injection (19%), insertion of an intravascular catheter (14%), and manipulation of an intravascular line (14%).

NEW PERILS

Of course, new perils always dot the horizon. Bovine spongiform encephalopathy (BSE) may be emerging as the newest terror in the workplace, especially in regions that have experienced this variant of Creutzfeldt-Jakob disease (CJD). Human cases in Great Britain prompted the Food and Drug Administration to issue restrictions on blood donations by individuals with prolonged residence in that country. Concerns were intensified by studies showing that unlike classic CJD, the etiologic prion protein of BSE can be found in lymphoreticular tissue.⁷⁹ Moreover, there has been a recent report of blood-borne transmission of BSE from an apparently healthy sheep that was incubating the disease to another sheep.⁸⁰ Nonetheless, there have been no documented cases of blood-borne cross-infection of either CJD or BSE in humans.

Regardless of what the future may hold with regard to the dangers of BSE in the workplace, one thing is certain. Adherence to the same prudent measures that have been relatively effective in reducing exposure to other blood-borne pathogens will be critical, and new approaches to further reducing the health care worker's risk clearly are needed.

REFERENCES

- Doebbeling BN, Pfaller MA, Houston AK, Wenzel RP. Removal of nosocomial pathogens from the contaminated glove: implications for glove reuse and hand washing. *Ann Intern Med* 1988;109:394-8.
- National Communicable Disease Center. Isolation techniques for use in hospitals. 1st ed. Washington (DC): US Government Printing Office; 1970. PHS Publication No. 2054.
- Trumbull ML, Greiner DJ. Homologous serum jaundice: an occupational hazard to medical personnel. *JAMA* 1951;145:965-7.
- Liebowitz S, Greenwald L, Cohen I, Litwinski J. Serum hepatitis in a blood bank worker. *JAMA* 1949;140:1331-3.
- Kuh C, Ward WE. Occupational viral hepatitis: an apparent hazard for medical personnel. *JAMA* 1950;143:631-5.
- Byrne EB. Viral hepatitis: an occupational hazard of medical personnel. *JAMA* 1966;195:362-4.
- Garner JS, Simmons BP. CDC Guideline for isolation precautions in hospitals. *Infect Control* 1983;4(Suppl 4):245-325.
- Centers for Disease Control. Recommendation for preventing transmission of infection with human T-lymphotropic virus type III/lymphadenopathy-associated virus in the workplace. *MMWR Morb Mortal Wkly Rep* 1985;34:681-6,691-5.
- Centers for Disease Control. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other blood-borne pathogens in health care settings. *MMWR Morb Mortal Wkly Rep* 1988;37:377-82,387-8.
- Lynch P, Jackson MM, Cummings MJ, Stamm WE. Rethinking the role of isolation practices in the prevention of nosocomial infections. *Ann Intern Med* 1987;107:243-6.
- Department of Labor, Occupational Safety and Health Administration. Occupational exposure to blood borne pathogens; proposed rule and notice of hearings. *Federal Register* 1989;54:23042-139.
- Department of Labor, Occupational Safety and Health Administration. Occupational exposure to blood borne pathogens; final rule. *Federal Register* 1991;56:64175-82.
- Garner JC, Hospital Infection Control Practices Advisory Committee. Guidelines for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996;17:53-80.
- Mahoney JE, Stewart K, Hu H, Coleman, Alter MJ. Progress toward the elimination of hepatitis B transmission among healthcare workers in the United States. *Arch Intern Med* 1997;157:2601-5.
- West DJ. The risk of hepatitis B infection among health professionals in the United States: a review. *Am J Med Sci* 1984;287:26-33.
- Gibas A, Blewett DR, Schoenfeld DA, Drensteg JL. Prevalence and incidence of viral hepatitis in health workers in the pre-hepatitis B vaccination era. *Am J Epidemiol* 1993;9:442-6.
- Beltrami EM, Williams IT, Shapiro CN, Chamberland ME. Risk and management of blood borne infections in healthcare workers. *Clin Microbiol Rev* 2000;13:385-407.
- Anonymous. Relation of antigen to infectivity of Hb_sAg-positive inoculations among medical personnel. *Lancet* 1996;2:492-4.
- Centers for Disease Control and Prevention. Outbreak of hepatitis B virus infection among hemodialysis patients-California. *MMWR Morb Mortal Wkly Rep* 1996;45:285-9.
- Werner BG, Grady GF. Accidental hepatitis-B-surface- antigen-positive inoculations: use of e antigen to estimate infectivity. *Ann Intern Med* 1982;97:367-9.
- Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *MMWR Morb Mortal Wkly Rep* 1998;47:1-39.
- Centers for Disease Control. Public Health Service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. *MMWR Morb Mortal Wkly Rep* 1991;40:1-17.
- Alter MJ. Epidemiology of hepatitis C. *Hepatology* 1997;26:625-55.
- McQuillan GM, Alter MJ, Moyer LA, Lambert SB, Margolis HS. A population based serologic study of hepatitis C virus infection in the United States. In: Rizzetto M, Purcell RH, Gerin JL, Vermer G, editors. *Viral hepatitis and liver disease*. Turin, Italy: Edizioni Minerva Medica; 1997. p. 267-70.
- Alter MJ. The epidemiology of acute and chronic hepatitis C. *Clin Liver Dis* 1997;1:559-68.
- Polish LB, Tong MJ, Co RL, Coleman PJ, Alter MJ. Risk factors for hepatitis C virus infection among healthcare personnel in a community hospital. *Am J Infect Control* 1993;21:196-200.
- Puro V, Petrosillo N, Ippolito G, Italian Study Group on Occupational Risk of HIV and Other Blood-borne Infections. Risk of hepatitis C seroconversion after occupational exposures in healthcare workers. *Am J Infect Control* 1995;23:273-7.
- Bradley DW, Krawczynski K, Beach MJ, Purdy MA. Non-A, non-B hepatitis: toward the discovery of hepatitis C and E viruses. *Semin Liver Dis* 1991;11:128-46.
- Davis GL, Law JYN. Hepatitis C. In: Haubrich WS, Schaffner F, Berk JE, editors. *Gastroenterology*. 5th ed. Philadelphia: WB Saunders and Co; 1995. p. 2082-114.

30. Santori M, LaTerra G, Aglietta M, Manzin A, Navino C, Verzetti G. Transmission of hepatitis C via blood splash into conjunctivae [letter]. *Scand J Infect Dis* 1993;25:270-1.
31. Ippolito G, Puro V, Petrosillo N. Simultaneous infection with HIV and hepatitis C virus following occupational conjunctivae blood exposure [letter]. *JAMA* 1998;280:28.
32. Chiarello IA, Gerberding JL. Human immunodeficiency virus in health-care settings. In: Mandell GL, Bennett JE, Dolin R, editors. *Mandell, Douglas and Bennett's principles and practices of infectious diseases*. 5th ed. New York: Churchill Livingstone; 2000; p. 3052-65.
33. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. *N Engl J Med* 1997;337:1485-90.
34. Tokars JJ, Chamberland ME, Schable A, Culver DH, Jones M, McKibben PS, et al. A survey of occupational blood contact with HIV infection among orthopedic surgeons. *JAMA* 1992;268:489-94.
35. Bell DM, Shapiro CN, Ciesielski C, Chamberland ME. Preventing blood borne pathogen transmission from healthcare workers to patients. *Surg Clin North Am* 1995;75:1189-203.
36. Harpaz R, Von Seidlein L, Averhoeff FM, Tormey MP, Sinha SD, Kotsopoulou K, et al. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. *N Engl J Med* 1996;334:549-54.
37. Duckworth GJ, Heptonstall J, Aitken C. Transmission of hepatitis C virus from surgeon to a patient. The Incident Control Team. *Commun Dis Public Health* 1999;2:188-92.
38. Esteban JI, Gomey J, Martell M, Cabot B, Quer J, Camps J, et al. Transmission of hepatitis C virus by a cardiac surgeon. *N Engl J Med* 1996;334:555-60.
39. Ross RS, Viazov S, Gross T, Hofmann F, Seipp H-M, Roggendorf M. Transmission of hepatitis C virus from a patient to an anesthesiology assistant to five patients. *N Engl J Med* 2000;343:1851-4.
40. Centers for Disease Control. Possible transmission of human immunodeficiency virus to a patient during an invasive dental procedure. *MMWR Morb Mortal Wkly Rep* 1990;39:489-93.
41. Danila RN, MacDonald KL, Rhame FS, Moen M, Reier DO, LeTourneau JC, et al. A look-back investigation of patients of an HIV-infected physician: public health implications. *N Engl J Med* 1991;325:1406-11.
42. Dickinson GM, Morhart RE, Klimas NG, Bandea CI, Laracuente JM, Bisno AL. Absence of HIV transmission from an infected dentist to his patients: an epidemiologic and DNA sequence analysis. *JAMA* 1993;269:1802-6.
43. Jaffe HW, McCurdy JM, Kalish ML, Liberti T, Metellus G, Bouman BH, et al. Lack of HIV transmission in the practice of a dentist with AIDS. *Ann Intern Med* 1994;121:855-9.
44. Mishu B, Schaffner W, Horan JM, Wood LH, Hutchenson RH, McNable PC. A surgeon with AIDS: lack of evidence of transmission to patients. *JAMA* 1990;264:467-70.
45. Rogers AS, Frogatt J III, Townsend T, Gordon T, Brown AJL, Holmes EC, et al. Investigation of potential HIV transmission to the patients of an HIV-infected surgeon. *JAMA* 1993;269:1795-801.
46. Von Reyn CF, Gilbert TT, Shaw FE, Parsonett KC, Abramson JE, Smith MG. Absence of HIV transmission from an infected orthopedic surgeon: a 13-year look-back study. *JAMA* 1993;269:1807-11.
47. Robert LM, Chamberland ME, Cleveland JL, Marcus R, Gooch BF, Srivastava PU, et al. Investigation of patients of healthcare workers infected with HIV: Centers for Disease Control and Prevention. *Ann Intern Med* 1995;122:653-7.
48. Kristensen MS, Wernberg NM, Anker-Moller E. Healthcare workers' risk of contact with body fluids in a hospital: the effect of complying with the universal precaution policies. *Infect Control Hosp Epidemiol* 1992;13:719-24.
49. Wong ES, Stotka JL, Chinchilli VM, Williams DS, Stuart CG, Markowitz SM. Are universal precautions effective in reducing the number of occupational exposures among healthcare workers? A prospective study of physicians on a medical service. *JAMA* 1991;265:1123-8.
50. Haiduvén DJ, Demaio TM, Stevens DA. A five-year study of needle stick injuries: significant reduction associated with communication, education, and convenient placement of sharp containers. *Infect Control Hosp Epidemiol* 1992;13:265-71.
51. Jagger J, Hunt EH, Bland-Elnaggar J, Pearson RD. Rates of needle stick injury caused by various devices in a university hospital. *N Engl J Med* 1988;319:284-8.
52. Mendelson MH, Short LJ, Schechter CB. Study of a needleless intermittent intravenous access system for peripheral infusions. Analysis of staff, patients, and institutional outcomes. *Infect Control Hosp Epidemiol* 1998;19:401-6.
53. Centers for Disease Control and Prevention. Evaluation of safety devices for preventing percutaneous injuries among healthcare workers during phlebotomy procedures. *MMWR Morb Mortal Wkly Rep* 1997;46:21-5.
54. Tokars JJ, Alter MJ, Favero MS, Moyer LA, Miller E, Bland LA. National surveillance of dialysis associated diseases in the United States, 1992. *ASAIO J* 1994;40:1020-31.
55. Gerberding JL, Littell C, Tarkington A, Brown A, Schechter WP. Risk exposure of surgical personnel to patients' blood during surgery at San Francisco General Hospital. *N Engl J Med* 1990;322:1788-93.
56. Panilio AL, Roy DR, Edwards JR, Bell DM, Welch BA, Parrish CM, et al. Blood contacts during surgical procedures. *JAMA* 1991;265:1533-7.
57. Popejoy SL, Fry DE. Blood contact and exposure in the operating room. *Surg Gynecol Obstet* 1991;172:480-3.
58. Panilio AL, Welch BA, Bell DM, Foy DR, Parrish CM, Perlino CA, et al. Blood and amniotic fluid contact sustained by obstetric personnel during deliveries. *Am J Obstet Gynecol* 1992;167:703-8.
59. Quebbeman EJ, Telford GL, Hubbard S. Risk of blood contamination and injury to operating room personnel. *Am Surg* 1992;214:614-20.
60. White MC, Lynch P. Blood contact and exposures among operating room personnel: a multi-center study. *Am J Infect Control* 1993;21:243-8.
61. Robert L, Short L, Chamberland M, McKibben P, Culver D, Srivastava P, et al. Percutaneous injuries sustained during gynecologic surgery [abstract]. *Infect Control Hosp Epidemiol* 1994;15:349.
62. Folin AC, Nordstrom GM. Accidental blood contact during orthopedic surgical procedures. *Infect Control Hosp Epidemiol* 1997;18:244-6.
63. Brough SJ, Hunt TM, Barrie WW. Surgical glove perforations. *Br J Surg* 1988;75:317.
64. McLeod GG. Needlestick injuries at operations for trauma: are surgical gloves an effective barrier? *J Bone Joint Surg Br* 1989;71:489-91.
65. Cole RP, Gault DT. Glove perforation during plastic surgery. *Br J Plast Surg* 1989;42:481-3.
66. Serrano CW, Wright J, Newton ER. Surgical glove perforation in obstetrics. *Obstet Gynecol* 1991;77:525-8.
67. Green SE, Gompertz RHK. Glove perforation during surgery: what are the risks? *Ann R Coll Surg Engl* 1992;74:306-8.
68. Chapman S, Duff P. Frequency of glove perforations and subsequent blood contact in association with selected obstetric surgical procedures. *Am J Obstet Gynecol* 1993;168:1354-7.
69. Rose DA, Ramiro N, Perlman J, Schechter WP, Gerberding JL. Usage patterns and perforation rates for 6396 gloves from intra-operative procedures at San Francisco General Hospital [abstract]. *Infect Control Hosp Epidemiol* 1994;15:349.
70. Gani JS, Anseline PF, Bissett RL. Efficacy of double versus single gloving in protecting the operating teams. *Aust N Z J Surg* 1990;60:171-5.
71. Doyle PM, Alvi S, Johanson R. The effectiveness of double gloving in obstetrics and gynecology. *Br J Obstet Gynaecol* 1992;99:83-4.
72. Matta H, Thompson AM, Rainey JB. Does wearing two pairs of gloves protect operating theatre staff from skin contamination? *BMJ* 1988;297:597-8.
73. Cohen MS, Do JT, Tahery DP, Moy DL. Efficacy of double gloving as a protection against blood exposure in dermatological surgery. *J Dermatol Surg Oncol* 1992;18:873-4.
74. Cohn GM, Seifer DB. Blood exposure in single versus double gloving during pelvic surgery. *Am J Obstet Gynecol* 1990;162:715-7.
75. Jensen SL, Kristensen B, Fabrin K. Double gloving as self-protection in abdominal surgery. *Eur J Surg* 1997;163:163-7.
76. Bennett B, Duff P. The effort of double gloving on frequency of glove perforations. *Obstet Gynecol* 1991;78:1019-22.
77. Dodds RDA, Barker SGE, Morgan NH, Donaldson DR, Thomas MH. Self-protection in surgery: the use of double gloves. *Br J Surg* 1990;77:219-20.
78. Schwimmer A, Massoumi M, Barr CE. Efficacy of double gloving to prevent inner glove perforation during outpatient oral surgical procedures. *J Am Dent Assoc* 1994;125:196-8.
79. Hill AF, Butterworth RJ, Joiner S, Jackson G, Rossor MN, Thomas DJ, et al. Investigation of variant Creutzfeldt-Jakob disease and other human prion diseases with tonsil biopsy samples. *Lancet* 1999;353:183-9.
80. Houston F, Foster JD, Chong A, Hunter N, Bostock CJ. Transmission of BSE by blood transfusion in sheep. *Lancet* 2000;356:999-1000.