

# 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

Health-care workers (HCWs) are potentially at risk for human immunodeficiency virus (HIV) infection through occupational exposures to blood. Although prospective studies indicate that the estimated risk for HIV infection after a percutaneous exposure to HIV-infected blood is approximately 0.3% (1,2), factors that influence this risk have not been determined. To assess potential risk factors, CDC, in collaboration with French and British public health authorities, conducted a retrospective case-control study using data reported to national surveillance systems in the United States, France, and the United Kingdom. This report describes the study and summarizes results that suggest that risk factors for HIV transmission include certain characteristics of the exposure and the source patient; in addition, postexposure use of zidovudine (ZDV) by HCWs was associated with a lower risk for HIV transmission. \*

Case-HCWs had a documented occupational percutaneous exposure to HIV-infected blood (i.e., a needlestick or a cut with a sharp object {e.g., scalpel or lancet}), HIV seroconversion temporally associated with the exposure, and no other concurrent exposure to HIV. Control-HCWs had a documented occupational percutaneous exposure to HIV-infected blood and were HIV seronegative at the time of exposure and at least 6 months later. Case-HCWs were identified through reports to national surveillance systems for occupationally acquired HIV infection operated by CDC, in cooperation with state and local health departments (United States), the National Public Health Network (Reseau National de Sante Publique) (France), and the Public Health Laboratory Service Communicable Disease Surveillance Center (United Kingdom). Control-HCWs were identified through reports to a passive surveillance project maintained by CDC since 1983 that includes data from approximately 300 health-care institutions in the United States (1).

The study included all case-HCWs reported in the United States whose exposure occurred during January 1988-August 1994 and all control-HCWs exposed after January 1988 whose 6-month follow-up evaluation was completed as of August 1994. Case- and control-HCWs reported in the United States before 1988 were excluded from the analysis because information on some variables was not routinely collected and because postexposure use of ZDV was infrequent before 1988 (1). For similar reasons, analysis was limited to case-HCWs reported in France since 1990 and in the United Kingdom since 1989.

Information obtained about HCWs included age; sex; occupation; work location; and whether postexposure antiretroviral agents were offered, whether they were used, how long after the exposure the first dose was used, daily dosage, and duration of treatment. Information about source patients included stage of HIV infection (acquired immunodeficiency syndrome {AIDS}, symptomatic, or asymptomatic), use of antiretroviral drugs at the time of the HCW's exposure, and presence of terminal illness (i.e., death because of AIDS within 2 months after the exposure). Information about exposures included the type of device involved, gauge of hollow-bore needle, type of procedure being performed, whether the procedure was an emergency, use of gloves, time from use of the device to exposure, presence of visible blood from the source patient on the device, and severity of injury. Severity of injury was defined as superficial (surface scratch, no blood appeared), moderate (penetrated skin and blood appeared), or deep (deep puncture or wound with or without bleeding).

The study included 31 case-HCWs (23 from the United States, five from France, and three from the United Kingdom) and 679 control-HCWs (who were from 190 of the reporting health-care institutions). Of the 31 exposures sustained by case-HCWs, 29 (94%) were needlesticks (all with hollow needles) and two (7%) involved other sharp objects. Of the 679 exposures sustained by control-HCWs, 620 (91%) were needlesticks (including 594 hollow and 26 solid needles) and 59 (9%) involved other sharp

objects.

For both case- and control-HCWs, 74% were exposed during 1990-1994, when ZDV postexposure use had become more common (1). During 1990-1994, 17 (81%) of 21 case-HCWs had been offered ZDV, and from September 1990 (when collection of information on whether ZDV was offered to control-HCWs became routine) through 1994, 268 (79%) of 338 control-HCWs were offered ZDV. ZDV postexposure prophylaxis was used by nine (29%) case-HCWs and 247 (36%) control-HCWs (crude odds ratio=0.7; 95% confidence interval {CI}=0.3-1.7). Regimens for case- and control-HCWs generally were 1000 mg/day for 3-4 weeks; the small number of case-HCWs who used ZDV precluded assessment of differences in ZDV regimens between case- and control-HCWs.

All variables that were statistically significant in the univariate analysis and variables potentially important for prevention (e.g., use of gloves, whether ZDV was offered, and whether ZDV was used) were examined using logistic regression analysis. Based on this analysis, factors associated with HIV transmission included a deep injury, device visibly contaminated with the source patient's blood, procedures involving a needle placed directly in a vein or artery, and terminal illness in the source patient. In addition, case-HCWs were significantly less likely to use ZDV than control-HCWs (adjusted odds ratio=0.2, *p* less than 0.01) ([Table 1](#)) \*\*. The crude odds ratio for ZDV use differed from the adjusted odds ratio because ZDV use was more frequent, among both case- and control-HCWs, for exposures characterized by the other factors. All factors in the model also were significant when the analysis was restricted to case-HCWs from the United States.

The degree of susceptibility to ZDV of HIV strains from source patients and case-HCWs is unknown. Information about antiretroviral treatment for source patients was available for seven case-HCWs and 124 control-HCWs who had used ZDV; five (71%) case-HCWs and 87 (70%) control-HCWs were exposed to blood from source patients who had been receiving ZDV at the time of the exposure.

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## Editorial Note

Editorial Note: The findings in this report indicate that, among the HCWs in this study, an increased risk for HIV infection following percutaneous exposures to HIV-infected blood was associated with three factors. First, the risk increased if the exposure involved a larger quantity of blood, indicated by 1) a device visibly contaminated with the patient's blood, 2) a procedure that involved a needle placed directly in a vein or artery, or 3) a deep injury. Second, the risk increased for exposures to blood from source patients with terminal illness, probably reflecting the higher titer of HIV in blood late in the course of AIDS or other factors, such as the presence of syncytia-inducing strains of HIV (3,4). Finally, the analysis of these data suggested that use of ZDV postexposure may be protective for HCWs. After controlling for other factors associated with HIV transmission risk, the model indicates that the risk for HIV infection among HCWs who used ZDV was reduced by approximately 79% (95% CI=43%-94%) (based on adjusted odds ratio=0.21; 95% CI=0.06-0.57). However, the limitations of the study design must be considered when interpreting these results.

A retrospective case-control study is not the optimal study design for assessing ZDV efficacy. The optimal approach -- a prospective, placebo- controlled trial -- 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 (1). The findings of this study also are subject to at least five potential limitations. First, case- and control-HCWs were identified using different data sources. Second, if control-HCWs were more likely to have been offered or encouraged to use ZDV, then use of the drug might be statistically associated with lack of HIV seroconversion, even if ZDV is not truly protective; however, available evidence does not suggest that control-HCWs were more likely than case-HCWs to have been offered ZDV. Third, reporting bias may have resulted if HCWs preferentially reported exposures that they believed were more likely to result in HIV transmission; this tendency presumably would be similar for case-HCWs and control-HCWs. Fourth, ascertainment bias may have affected some data, particularly subjective variables such as severity of injury, because information for control-HCWs was obtained prospectively soon after exposure but information for most case-HCWs was obtained after HIV seroconversion; however, for most variables evaluated, objective documentation from incident reports and medical records was available. Finally, number of case-HCWs evaluated was small.

Although failures of postexposure ZDV to prevent HIV infection in HCWs have been documented (1), this is the first study of

HCWs exposed to HIV that assesses the effectiveness of ZDV as postexposure prophylaxis. Studies involving animals have yielded inconclusive results (5). In studies involving humans, ZDV was reported to reduce the rate of perinatal HIV transmission (6) and to be beneficial in treating early HIV infection (7); however, the implications of these results for postexposure prophylaxis are uncertain. The short-term toxicity of ZDV in HCWs primarily has been gastrointestinal discomfort and fatigue (1,2,5,8).

ZDV is not approved by the Food and Drug Administration for use as postexposure prophylaxis. In a previous statement, the Public Health Service (PHS) concluded that a recommendation could not be made for or against the use of ZDV postexposure prophylaxis because of limited knowledge regarding its efficacy and toxicity (9). PHS recommends that HCWs who may be at risk for occupational exposure to HIV infection be informed of the considerations pertaining to the use of ZDV for postexposure prophylaxis, including the risk for HIV transmission after the exposure, factors that may increase or decrease this risk, and the limited knowledge regarding the potential efficacy and toxicity of ZDV postexposure prophylaxis (9). If a decision is made to use postexposure prophylaxis, it should be initiated promptly (9). PHS is evaluating the implications of the study summarized in this report and other available information in assessing the possible need for revision of recommendations for managing occupational exposure to HIV -- particularly regarding postexposure use of antiretroviral agents.

## References

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Single copies of this report will be available free until December 21, 1996, from the CDC National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003; telephone (800) 458-5231 or (301) 217-0023. \*\* Information on terminal illness in the source patient was missing for 19% of case-HCWs and 48% of control-HCWs; information on visible blood on device was missing for 3% of case-HCWs and 6% of control-HCWs. By recoding the missing values to zero and including missing value indicator variables for these factors in the model, these HCWs were retained in the analysis and their potential confounding influence could be assessed. No significant interactions were found among the risk factors in the model or between the risk factors and the missing value indicators. When all HCWs with missing values for any of the factors were excluded from the analysis, all of the factors remained significant, with similar adjusted odds ratios but larger confidence intervals.

## Table\_1

**Note:** To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

TABLE 1. Risk factors for HIV infection in health-care workers after percutaneous exposure to HIV-infected blood, based on a case-control study -- France, United Kingdom, and United States, January 1988-August 1994

Risk factor	Adjusted odds ratio *	(95% CI +)
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Deep injury	16.1	(6.1-44.6)
Visible blood on device	5.2	(1.8-17.7)
Procedure involving needle placed directly in a vein or artery	5.1	(1.9-14.8)
Terminal illness in source patient	6.4	(2.2-18.9)
Postexposure use of zidovudine	0.2	(0.1- 0.6)

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 \* All were significant at p<0.01. + Confidence interval.="-----"

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