



Occupational Exposures to Retroviruses

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Abstract

In the scientific community laboratory workers have recently been concerned about their increased risk for infection by viruses. In view of the AIDS epidemic, one family of viruses that has required vigilant surveillance has been the retroviruses. Their stealthy infectious course of genomic integration followed by a long latent period culminating in disease is especially dangerous to public health. As new areas of health care become a standard practice of medicine (xenotransplantation, gene therapy, genetically engineered vaccines, etc.), greater attention must be given to identifying transmission of newly emerging retroviruses from these procedures.

In 1995, the Centers for Disease Control and Prevention (CDC) began systematic, prospective surveillance to identify and characterize potential transmission sources of such agents in occupational settings where humans may come in contact with nonhuman primates. Much of this activity resulted from an awareness that human immunodeficiency virus (HIV) came from nonhuman primates and that greater effort to develop an HIV vaccine would potentially place more animal workers at risk from viruses transmissible from nonhuman primates to humans. This article addresses emerging retroviruses in general and the occupational safety issues for laboratory workers who come in contact with nonhuman primates and their tissues.

Emergence of Viruses

The emergence of viruses and their diseases typically occurs in one of two ways: agents may reemerge by rapidly increasing in incidence or geographic

range after having been controlled (e.g., ebola), or the agents may be recognized as completely new (e.g., hepatitis C). Since 1988, nearly 70 new viruses or viral-like agents that affect humans could be identified as "emerging." This number represents an increase of nearly five new agents per year. A major factor in the role of emergence and reemergence of these microbes is human behavior. Although virus evolution and adaptation are other main contributors to this phenomenon, human behavior begins the process. In addition, a few other human components—such as international travel and commerce, breakdown in public health measures, changes in technology, and economic development coupled with land use—determine the extent to which emerging opportunities can develop.

Factors other than human elements also predispose a new virus to emerge. First, mutation, reassortment, and recombination are primary features necessary for a new agent to adapt. Second, the host may be modified in such a way that a new virus gets a "foothold," such as with a susceptibility factor like immunosuppression. Finally, increasing contact with a new agent by invading its ecological niche can create additional selective opportunities for infection. Only through vigilant surveillance established in a proactive setting can an emerging virus be thwarted from resulting in an emerging epidemic.

Surveillance of Emerging Retroviruses

Surveillance for newly emerging HIVs is one of the primary responsibilities of the HIV and Retrovirology Branch at CDC. As a result of the Human Immunodeficiency Virus-1 (HIV-1) pandemic, extensive efforts have been made toward developing new

generic retroviral detection tools to investigate the potential for a new HIV to surface (Heneine, Yamamoto, Switzer, et al., 1995). Since peaking in 1994, the number of deaths from HIV/AIDS in the United States has steadily declined because of new drug therapies. However, the rate of new infections continues to be an important control and prevention problem. One of the primary reasons that retroviruses are so dangerous is the long clinical latent period that persists following infection. One biological reason for this long period is the ability of retroviruses to integrate their genome into the host's genetic material, thus providing a secure, sequestered copy of the viral genome for generations of cell divisions. This aspect of the biology of retroviruses makes their infectious process especially harmful to the safety of public health.

Biomedical Areas Associated with Risks for Retroviral Transmission

To identify emerging retroviruses, investigations are taking place in our laboratory in four important areas of biomedical research:

1. Gene therapy
2. Xenotransplantation
3. Vaccines and vaccine substrates

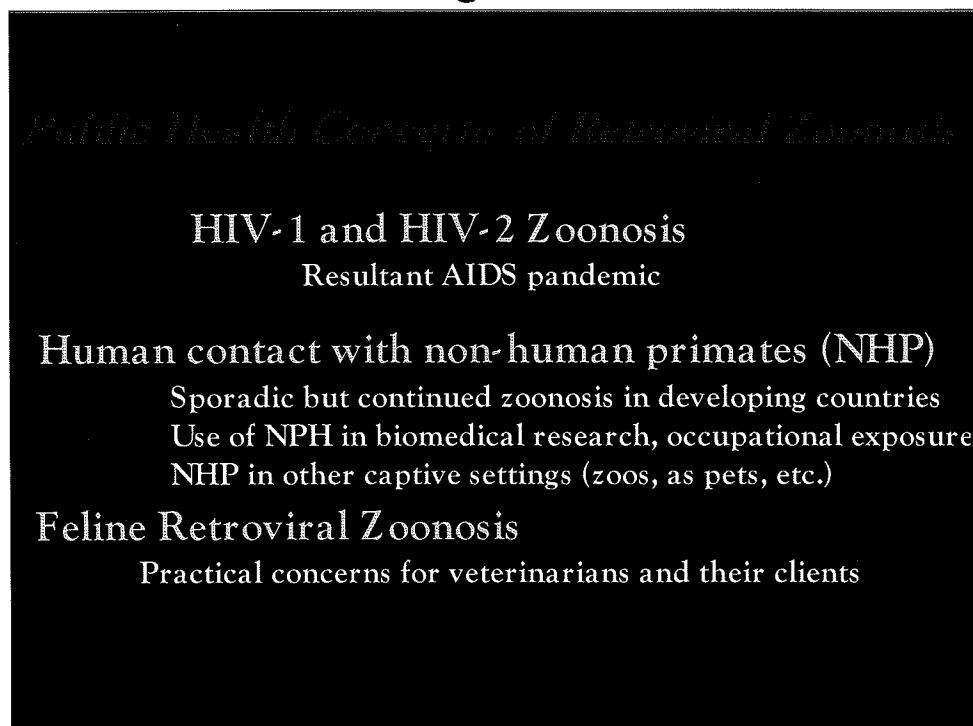
4. Zoonosis (occupational exposures)

Although the following discussion focuses on zoonosis, the areas of gene therapy and xenotransplantation are rapidly becoming standard practices of medicine and vigilant surveillance will certainly be needed to detect emerging infectious agents (Boneva, Folks, & Chapman, 2001; CDC Policy Working Group and PHS Interagency Committee on Xenotransplantation, 1998; Chapman, Solomon, Patterson, et al., 1995; Heneine, Switzer, Soucie, et al., 2001; Hussain, Shanmugam, Switzer, et al., 2001; Matthews, Brown, Switzer, et al., 1999).

Public Health Concerns About Retroviral Transmission in Occupational Settings

Two areas of zoonosis have been the focus of CDC's surveillance for emerging retroviruses in occupational settings: feline-to-human retroviral transmissions and human contact with nonhuman primates (Figure 1). For years we have understood that veterinarians encounter frequent risks for zoonosis from common household pets. In a study of occupational exposures of feline practitioners, 203 individuals were anonymously assayed for three classes of feline retroviruses: feline immunodeficiency syn-

Figure 1



drome, feline leukemia virus, and feline foamy virus (FFV) (Butera, Brown, Callahan, Owen, et al., 2000). Of the 203 individuals, nearly 9% reported high-risk exposures to cats (including blood exposure on broken skin and face splashes with feline blood, urine, or feces) and puncture wounds from venipunctures, bone marrow aspirates, and orthopedic procedures. The samples of all individuals tested negative by serology (all three virus types) and PCR (FeLV). We concluded that the risk for feline zoonosis among otherwise healthy adults is extremely small or nonexistent. However, we would caution that risks could still exist, especially for the young, elderly, and immunocompromised. Furthermore, we recommend that universal precautions always be adopted when approaching cats known to be viremic.

Transmission and Divergence of HIV

AIDS as a zoonosis is a concept well accepted by the scientific community. Although it is uncertain how HIV-1 moved to the human species from nonhuman primates, most of the community agrees that at some point HIV was linked to its close cousin, simian immunodeficiency virus (SIV), which has been reported in over 26 different species of African nonhuman primates (Gao, Balles, Robertson, et al., 1999; Hahn, Shaw, De Cock, et al., 2000). After ani-

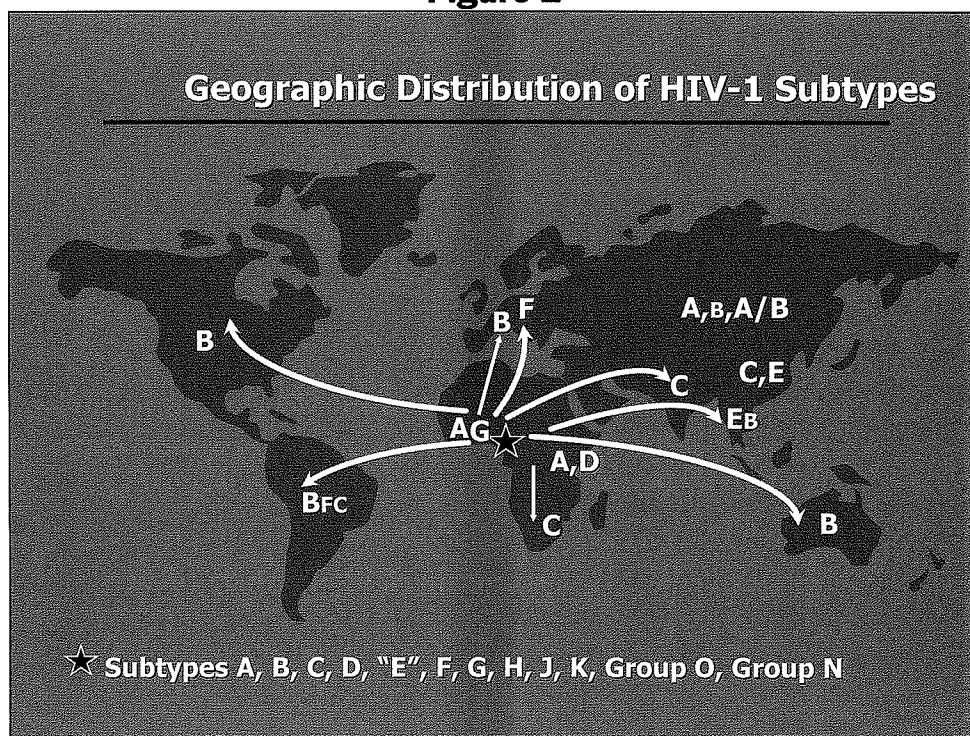
mal-to-human transmission and adaptation in central Africa, HIV-1 diverged into three groups, designated M, O, and N (Simon, Maule, Rogues, Loussert-Ajaka, Muller-Trutwin, Saragosti, Georges-Courbot, Barre-Sinoussi, & Brun-Vezinet, 1998). The major group, M, has further diverged into 10 subgroups or clades (A-K). Although all these subgroups are found in central Africa, they have spread as separate clades to seed the AIDS epidemic worldwide (Figure 2) (Korber, Muldoon, Theiler, et al., 2000). The insidious nature of these viruses and their unchecked, silent movement through the population remain a continuing public health worry.

Development of Biosafety Guidelines

Concerned that contact between nonhuman primates and humans might spark a new retroviral epidemic, CDC developed the first biosafety guidelines for working with nonhuman primates and material derived from them (Centers for Disease Control and Prevention, 1988). Although nonhuman primates are natural hosts for a number of exogenous viruses (SV40, Herpes B), the primary focus of our work was to survey workers occupationally exposed to the four known simian retroviruses:

1. SIV, which was known to be prevalent in African primates, is often asymptomatic in its natural

Figure 2



host but can cause AIDS-like disease in a susceptible primate.

2. Simian type D retrovirus (SRV-D), which is prevalent in Asian macaques and baboons, can also cause an AIDS-like disease or fibrosarcoma.

3. Simian T-cell leukemia virus (STLV), which is highly prevalent in captive monkeys, can cause leukemia and is associated with outbreaks of lymphoma in primate colonies.

4. Simian foamy virus (SFV) is not known to cause disease in its natural host but is highly prevalent in captive primates, at times infecting 100% of a colony.

Timeline of CDC Intervention/ Surveillance Efforts

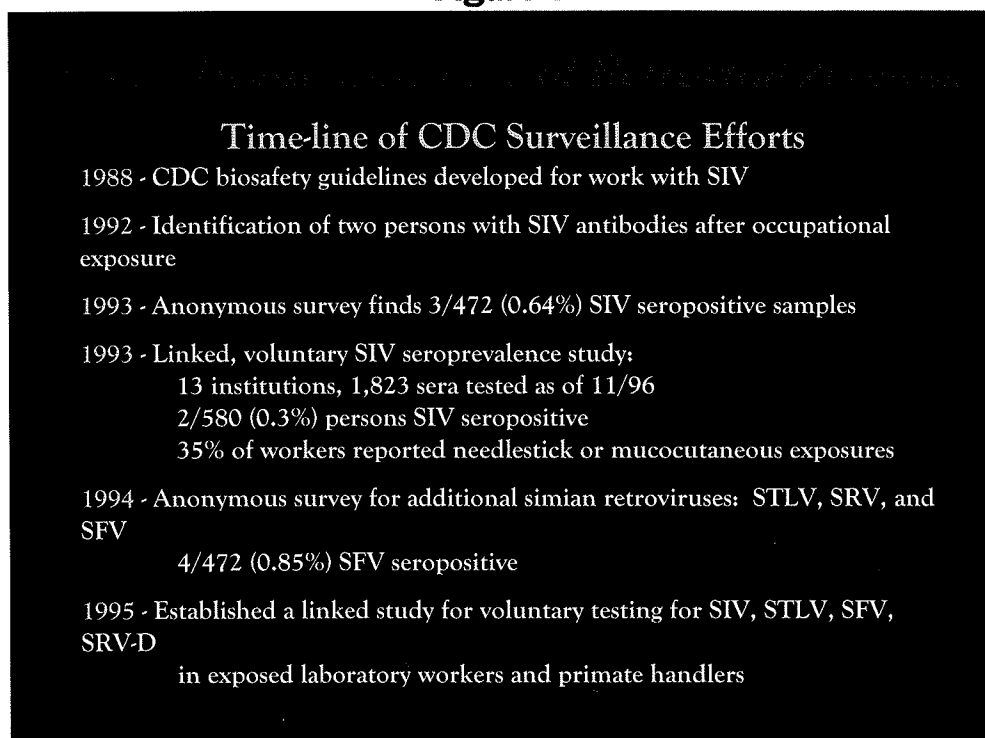
The 1998 CDC guidelines called for the same universal precautions that were recommended for working with human blood and tissues. At the time, we believed that transmission of simian viruses, including the retroviruses, could cross species barriers and infect humans. Then in 1992, CDC identified two individuals who had antibodies to SIV after reports of accidental exposure to nonhuman primates (Centers for Disease Control and Prevention, 1992). In 1993, CDC and the National Institutes of Health

conducted an anonymous survey of 472 animal care and laboratory workers to determine the number of individuals who might have antibodies to SIV. The study found three (0.64%) individuals to be seropositive for SIV (these positive individuals may have been the same individuals identified in the first study) (Centers for Disease Control and Prevention, 1992).

These findings led to a linked, prospective, voluntary study later in 1993 to better understand SIV seroprevalence in this population. Thirteen institutions were enrolled, 1,823 specimens were collected from animal care and laboratory workers, and tests were performed for antibodies to SIV. (By November 1996, two positive samples had been detected from 580 persons [0.3%.]) A total of 35% of the workers reported needlestick or mucocutaneous exposures (Khabbaz, Rowe, Murphy-Corb, et al., 1994; Khabbaz, Heneine, George, et al., 1994).

In 1994, our laboratory began another anonymous serologic survey to determine the prevalence of other simian retroviruses (SRV, STLV, and SFV) in this population of workers. This study revealed a surprising emergence of a new family of viruses in humans. Although no seropositive results for STLV or SRV were identified, a striking 0.85% of the individuals (4 out of 472) were seropositive for SFV (Heneine, Switzer, Sandstrom, et al., 1998; Sand-

Figure 3



strom, Phan, Switzer, et al., 2000). As a result of these findings, CDC established a linked, prospective study in 1995 involving voluntary testing for all four simian retroviruses in exposed laboratory workers and primate handlers (Figure 3).

Studies in Progress

Since 1995 we have established a protocol for long-term follow-up of these infected workers and a look-back study to identify infected individuals who may have been blood donors. To date, none of the individuals infected with SIV or SFV has shown signs or symptoms of disease. In addition, no transmission of these viruses from human to human, either sexually or through blood transfusion, has been found (Boneva, Grindon, Orton, et al., 2002). CDC continues to offer serological screening of occupationally exposed workers. To address potential SIV transmission to animal and laboratory workers, we have begun establishing a list of antiretroviral drugs that would be useful as post-exposure prophylaxis in the event of an accident. The current recommendation is to avoid non-nucleoside reverse transcriptase inhibitor analogues to treat an acute exposure, since SIV is known to be naturally resistant to this class of drugs.

Our continued goal is to provide expanded surveillance for emerging retroviruses and to offer screening of high-risk individuals, especially those in occupations involving laboratory work or animal/primate handling. Overall, our studies of these populations can help clarify the pathogenic potential and secondary transmissibility of emerging retrovirus infections in humans. And, more importantly, this work will provide safety information to help protect workers.

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