

Lessons from an HIV Transmission Pair

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(See the editorial commentary by Allos and Schaffner, on pages 1245–7; the major article by Blick et al., on pages 1250–9; and the brief report by Redd et al., on pages 1311–4.)

In February 2006, the New York City Health Department held a press conference to issue a public health alert involving the transmission of a highly drug-resistant HIV variant that appeared to be associated with rapid disease progression. As the recently infected individual had potentially exposed dozens of other men, the Health Department felt it was necessary to alert the public about the potential risk of this HIV variant and to urge partners to obtain testing. The press conference sparked controversies and raised public concern about the spread of a new HIV “superbug.” The article by Blick et al. in this issue of the *Journal* helps illuminate some of these controversies, while raising potential new controversies of its own [1].

One controversy was just how rapid the disease progression was in the newly infected “NYC patient.” The NYC patient’s last negative HIV test was performed 15 months before his HIV diagnosis [2]. At HIV diagnosis his CD4⁺ T cell count was <100 cells/ μ L. On the basis of the patient’s history, those reporting the case believed

that he had been infected only a few months before diagnosis. A less-sensitive EIA test was already reactive, however, providing no evidence to support recent infection and suggesting that he had been infected at least a few months. The report by Blick et al. provides strong evidence that the NYC patient was infected <2 months before his diagnosis. The evidence comes from identification of the source or donor partner (“CT01”) and interview data that identifies the exact date on which transmission presumably occurred.

The second issue that the Blick et al. report addresses is whether the HIV variant in the NYC patient is consistently associated with rapid progression. CT01 had a similar HIV variant but did not show the same type of rapid progression. This suggests that host factors as well as, or instead of, the virus were important in the pace of NYC’s disease progression. The reassurance this provides about the virulence of the HIV variant is partially tempered by the fact that CT01 had only been known to be infected for 2 years before starting antiretrovirals. Exactly how rapidly he would have progressed without treatment is still open to question. It is also possible that evolution to a more virulent viral variant occurred after treatment was started.

The Blick et al. report is noteworthy for another reason: it provides strong evidence that CT01’s primary partner (“CT02”) became superinfected with a drug-resistant

variant transmitted by CT01. The evidence comes from viral genetic data from serial genotyping showing the appearance of a new viral variant in CT02 that was highly divergent from an earlier genotype but that closely matched that of CT01. Further evidence for superinfection comes from subsequent genotypes that appear to represent a recombinant virus containing a segment of CT02’s initial virus combined with part of CT01’s viral variant.

Serosorting, or the use of information about HIV status in the selection of sex partners and the decision about whether to use condoms and other safer sex steps with the partner, has been considered a potentially important measure to reduce HIV transmission [3, 4]. We believe that existing evidence continues to suggest that superinfection with systemic expression of a second HIV variant is uncommon after the first few years of infection, and this report should not lead to the abandonment of serosorting as one strategy to reduce HIV transmission. However, this case is an important cautionary tale that drug-resistant HIV truly can be transmitted to a chronically HIV-infected partner. Prior reports of HIV superinfection have documented transmission of drug-resistant HIV and potential rapid disease progression in early HIV infection [5]. Health care providers who counsel HIV-infected patients now need to insure that patients are aware that acquisition of drug-resistant HIV through unprotected sex is possible

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in chronic HIV infection, although the magnitude of the risk remains uncertain. Further study to more fully characterize the level of risk and predictors of superinfection is urgently needed to inform public health policies and to advance our understanding of HIV transmission biology and protective immunity.

There is another aspect of the report by Blick et al. that may prove more disquieting to medical providers and our patients than the documentation of superinfection with drug-resistant HIV during chronic infection: the process through which CT01 was identified as the probable source of NYC's HIV infection. The alert issued by the New York City Health Department prompted a search of commercial HIV drug-resistance genotyping databases, which eventually led to the identification of CT01 as the source. The use of such databases is a potentially powerful tool for public health purposes. As with all such powerful tools, how this gets used and the confidentiality protections that are put in place are critical.

Public health officials have broad authority to undertake investigations to protect public health. They may access medical records without patient consent. HIV genotyping may be an important tool in identifying and responding to potential threats to public health, such as the source of a highly drug-resistant, rapidly progressing HIV strain. Public health officials have a strong history of protecting sensitive, confidential information obtained in the course of their duties.

The justifications for allowing public health officials access to confidential medical tests for public health practice do not carry over when findings will be published and the purpose of the activity shifts from disease surveillance and prevention to contributing to generalizable knowledge. Systematic efforts to develop generalizable knowledge ordinarily constitute "research" under the federal regulations governing human subjects research [6]. Human subjects research typically requires institutional review board (IRB) approval

and consent. However, much review of existing records may be exempt from consent if identifiable information is not recorded [7].

Case studies typically do not require IRB review because they are not "systematic investigations" that yield generalizable knowledge. Although they may be published without patient permission provided patient identity is adequately protected, it is ethically preferable to obtain patients' consent.

The CT01 report raises much more complex issues than usual case histories. The report involves not only the patient's history, but it is noteworthy in large part because of the linkage to another patient. In a report such as this, HIV genotyping related to identifiable individuals could potentially lead to civil or criminal actions for exposure to HIV [8]. It is therefore essential that the consent process is robust and truly voluntary. Source patients need to understand that, although they may be required to participate in the public health investigation, they can refuse permission to use their information in publications. They also should be told what information may be published, what steps are being taken to protect their confidentiality, and how it might be possible to infer their identity because of the unusual circumstances of the case, even if they are not explicitly identified in the publication. This is especially important because sharing genotyping information with publicly accessible databases, such as GenBank, as part of the research publication could make it easier to reidentify subjects using other databases. Steps must be taken to ensure that publishing important public health information does not put source patients in legal jeopardy. Reports should include the minimum scientifically necessary information about the source patients and careful attention to anonymization of data. In some cases, it may be advisable to withhold or obscure factual information for added protection.

The involvement of source patients' physicians in research presents unique

ethical concerns. Although physicians can play an important role in informing and counseling patients identified as a source of infection, most do not have the same experience as public health officials in conducting public health investigations. In some states, information maintained by physicians may have less legal protection than public health records and, therefore, could reduce protection for source patients. For example, in some states public health records may not be used as evidence in legal proceedings, whereas a court may allow medical records to be subpoenaed [9, 10]. The treating physician's involvement itself may also provide clues to the source patient's identity by suggesting where the patient lives and receives medical care. Finally, if, as in this case, the determination is made to publish results from a public health investigation, the treating physician's role as an author may compromise the ability to obtain truly voluntary informed consent because it may be difficult for a patient to refuse a personal physician's request. Patients may feel obligated to agree either out of affection for their physician or fear that their care will suffer if they refuse.

Even if not required, IRB review could have strengthened protections for source patients in a case like this one. For example, an IRB may have suggested a certificate of confidentiality, which protects identifiable, sensitive research data against compelled disclosure in any legal proceeding [11]. IRBs can also help public health officials determine when they cross the line from practice to research and how best to protect patients when they publish case reports.

This case provides important information about HIV transmission and superinfection, but also highlights potential risks to individuals if genotyping data are used for purposes other than selecting an antiretroviral treatment regimen. Public health officials, physicians, and persons with HIV infection need to discuss how to optimize the benefits of HIV genotype testing for clinical purposes, while ad-

addressing the ethical and legal concerns about other uses of these data.

References

1. Blick G, Kagan RM, Coakley E, et al. The probable source of both the primary multidrug-resistant (MDR) HIV-1 strain found in a patient with rapid progression to AIDS and a second recombinant MDR strain found in a chronically HIV-1-infected patient. *J Infect Dis* **2007**;195:1250–9 (in this issue).
2. Markowitz M, Mohri H, Mehandru S, et al. Infection with multidrug resistant, dual-tropic HIV-1 and rapid progression to AIDS: a case report. *Lancet* **2005**;365:1031–8.
3. San Francisco serosorting may explain odd HIV data: STDs have risen, but not new HIV infections. *AIDS Alert* **2004**;19:55–6.
4. Parsons JT, Schrimshaw EW, Wolitski RJ, et al. Sexual harm reduction practices of HIV-seropositive gay and bisexual men: serosorting, strategic positioning, and withdrawal before ejaculation. *AIDS* **2005**;19(Suppl 1): S13–25.
5. Smith DM, Richman DD, Little SJ. HIV superinfection. *J Infect Dis* **2005**;192:438–44.
6. 45 C.F.R. §46.102 (2006).
7. 45 C.F.R. §46.101(b)(4) (2006).
8. Wolf L, Vezina R. Crime and punishment: is there a role for criminal law in HIV prevention policy? *Whittier Law Rev* **2004**;25:821–86.
9. Conn. Gen. Stat. §19–25 (2006) (public health records inadmissible).
10. Conn. Gen. Stat. §19a-583 (2006) (permitting court-ordered release of HIV-related information).
11. Wolf L, Zandecki J, Lo B. The certificate of confidentiality application: a view from the NIH institutes. *IRB* **2004**;26:14–8.