AIDS

CDC's Investigation of HIV Transmissions by a Dentist
Chairman
Human Resources and Intergovernmental Relations Subcommittee
Committee on Government Operations
House of Representatives

Dear Mr. Chairman:

On July 27, 1990, the Centers for Disease Control (CDC) reported that a young woman had possibly been infected with the human immunodeficiency virus (HIV) by a dentist with acquired immune deficiency syndrome (AIDS). In 1991, CDC concluded that five patients became infected while receiving care from the dentist and that the mode of transmission remains uncertain.

Our report responds to the request of the former chairman, the Honorable Ted Weiss, that we assess the methods and evidence CDC used in answering the two questions of its investigation:

- Did the dentist transmit HIV to his patients?
- How did the HIV transmission occur?

We reviewed CDC's investigation to determine whether its methods were sound as well as whether the evidence they accumulated adequately supports the findings.

We will be sending copies of this report to the Secretary of Health and Human Services, the Director of CDC, and to other interested parties. We will also make copies available to others upon request.

If you have any questions or would like additional information, please call me at (202) 275-1854 or Robert L. York, Director of Program Evaluation in Human Services Areas, at (202) 275-5885. Other major contributors to this report are listed in appendix I.

Sincerely yours,

Eleanor Chelimsky
Assistant Comptroller General
Executive Summary

Background and Purpose

The Centers for Disease Control (CDC) reported on June 14, 1991, that its investigation “strongly suggests that five patients became infected while receiving care from a dentist with AIDS.” These are the first and only reported cases of the transmission of the human immunodeficiency virus (HIV) from a health care worker to patients. Reacting to these cases, on July 12, 1991, CDC issued guidelines intended to prevent such transmission in the future. These guidelines have proven to be contentious, and CDC was in the process of clarifying them as of June 1992.

The Human Resources and Intergovernmental Relations Subcommittee of the House Committee on Government Operations requested on October 22, 1991, that the U.S. General Accounting Office (GAO) conduct an inquiry into CDC’s handling of this matter. Specifically, the Subcommittee asked GAO to examine (1) the appropriateness and adequacy of CDC’s investigation of the Florida dentist and his office practices, (2) the evidence on which CDC based its conclusions regarding the mode of transmission from the dentist to his patients, and (3) the methodology and process CDC used and the support for its guidelines concerning HIV-positive health care workers.

The status of CDC’s guidelines regarding HIV in the health care workplace has remained in flux since receipt of the Subcommittee’s request. Therefore the Subcommittee agreed that in this report GAO would address in detail only the first two questions.

Results in Brief

Although GAO identified minor problems, CDC’s investigation as a whole was found to have been both thorough and competent. The evidence GAO reviewed supports CDC’s conclusions that five patients became infected while receiving care from a dentist with acquired immunodeficiency syndrome (AIDS) and that the mode of transmission remains uncertain. That the mode of transmission remains unknown means that this case provides little specific information to advance understanding of how to prevent such occurrences in the future.

Principal Findings

Source of Infection

CDC conducted field and genetic investigations to determine whether the dentist infected five patients. CDC’s analysts held numerous interviews with
the infected patients concerning their potential exposure to HIV and attempted to corroborate this information by other sources. For at least some of these patients, the dental practice was the only potential exposure to HIV that could be confirmed. For none of the patients could the possibility of infection from other sources be definitively excluded, however.

CDC also examined genetic material (DNA) from the HIV of the dentist, the infected patients, and other HIV-positive individuals in the local area. Multiple tests indicated that the dentist and the five patients had similar strains of HIV that were distinct from those of the other individuals. The DNA from the dentist and the five patients was as similar as for individuals known to have a common source of infection. This finding serves as the basis for concluding that the dentist was the common source of the infections.

The principal problem GAO found with CDC's genetic study was that, at least initially, the researchers knew which data came from the dentist and which came from the first patient. Data from the dentist were labeled as such, and data from the patient were labeled as such. Whenever research data are labeled, there is always concern about bias entering into data analysis.

**Mode of Transmission**

There is no certainty regarding the mode of transmission. The most likely of several explanations investigated is that the patients were infected through exposure to the dentist's blood. The dentist performed invasive dental procedures on each patient, and these procedures provided multiple opportunities for the dentist to have injured himself and then come into contact with the patients' blood. There is no record that the dentist became injured while treating these patients, however, and neither these patients nor the dentist could recall any such injuries.

Other modes of transmission are also possible. Available evidence gives no indication that the patients contracted HIV through sources outside the dental office, through sexual contact with the dentist or contaminated dental equipment, or because the dentist had an especially virulent form of HIV. With the exception of one interview with an acquaintance of the dentist, the various interviews with the dentist, his family, dental staff, health care workers, patients, and other acquaintances provided no evidence that transmission was intentional.
Executive Summary

CDC did not use a dental specialist in its one interview with the dentist. A dentist might have asked follow-up questions about specific dental procedures. Questions from a dental epidemiologist might have provided additional information about the dental practice that could have been helpful in identifying how the infections occurred.

CDC Guidelines

CDC's guidelines for preventing HIV transmission in health care settings attempt to prevent future infection of patients by HIV-positive health care workers. But because CDC was unable to determine precisely how the virus was transmitted, the case of the Florida dentist furnishes only sparse information on which to base policy seeking to prevent such occurrences. For example, the investigation of the dental practice failed to show that certain medical procedures are riskier than others in terms of HIV transmission.

Prior to its investigation, CDC had suggested that the transmission of HIV from health care workers to patients would occur "only very rarely, if at all." The incidents involving the Florida dentist and five of his patients certainly appear to demonstrate that such transmission is more than a theoretical possibility. Yet other studies of over 15,000 patients treated by HIV-positive health care workers have thus far failed to demonstrate even a single additional health care worker-to-patient transmission.

As a consequence, the public policy implications of this one outbreak of HIV in a health care setting are unclear. That is, with respect to the CDC guidelines regarding HIV-positive health workers that have already been issued and are currently being reconsidered, GAO is concerned that all the scientific information needed to formulate an effective prevention policy may not yet be available. As already noted, the specific mode of HIV transmission to the patients could not be identified, and in addition, the precise circumstances that resulted in transmission to multiple patients in a single practice remain unknown.

Recommendations

Although GAO finds that CDC's investigation of the Florida dentist's case was well done, it appears that the marshaling of evidence in CDC's future work involving HIV in the health care workplace could be improved in two ways. GAO recommends that the Director of CDC (1) ensure that all relevant expertise is used when investigating new potential sources of HIV infection and (2) avoid potential bias in its analyses regarding HIV by masking the identity of the persons from whom genetic material is obtained.
Agency Comments

At the request of the Subcommittee, GAO did not obtain written comments from the Department of Health and Human Services. However, officials from the Centers for Disease Control were briefed on GAO's major findings and conclusions.
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### Abbreviations

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<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
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<td>AZT</td>
<td>Zidovudine</td>
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<td>CDC</td>
<td>Centers for Disease Control</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>GAO</td>
<td>U.S. General Accounting Office</td>
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<td>HBV</td>
<td>Hepatitis B virus</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HLA</td>
<td>Human leukocyte antigen</td>
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<td>HRS</td>
<td>Florida Department of Health and Rehabilitative Services</td>
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<td>IV</td>
<td>Intravenous</td>
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<td>LANL</td>
<td>Los Alamos National Laboratory</td>
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<td>LC</td>
<td>Local control</td>
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<td>MMWR</td>
<td>Morbidity and Mortality Weekly Report</td>
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<td>PCR</td>
<td>Polymerase chain reaction</td>
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Objectives

On July 27, 1990, CDC first reported that a young woman had possibly been infected with HIV by a Florida dentist with AIDS.\(^1\) Over the next year CDC attempted to determine whether HIV had indeed been transmitted through this dental practice. On June 14, 1991, CDC concluded that its investigation “strongly suggests that [a total of] five patients became infected while receiving care from a dentist with AIDS.”\(^2\) These are the first and only reported cases of transmission of HIV from a health care worker to patients. Reacting to these cases, on July 12, 1991, CDC issued guidelines intended to prevent such transmission in the future. Because these guidelines have been contentious, CDC was in the process of clarifying them as of June 1992.\(^3\)

The Human Resources and Intergovernmental Relations Subcommittee of the House Committee on Government Operations asked us on October 22, 1991, to inquire into CDC’s handling of this matter. The Subcommittee requested that we examine the appropriateness and adequacy of CDC’s investigation of the dentist and his office practices, the evidence on which CDC based its conclusions regarding the mode of transmission from dentist to patient, the process CDC used to issue its guidelines, and the support for these guidelines.

This study assesses the methods and evidence CDC used in answering two substantive questions:

1. Did the dentist transmit HIV to his patients?

2. How did the HIV transmission occur?

In assessing CDC’s inquiry regarding these questions, we also attempted to answer two methodological questions:

1. Were CDC’s methods sound?

2. Does CDC’s evidence adequately support its findings?

\(^1\)A person is diagnosed with AIDS based on manifesting a variety of AIDS-related maladies. The diagnosis of HIV is made through blood tests that show the presence of antibodies to HIV. We refer throughout to HIV-infected individuals as being “HIV-positive.” HIV causes AIDS.


CDC was clarifying its guidelines regarding HIV in the health care workplace at the time this report was prepared. We are monitoring CDC's work on the guidelines, and we do not comment on it in this report. We do, however, consider the extent to which the investigation of the Florida dentist provides information useful in developing guidelines for health care workers with HIV.

We address the substantive and methodological questions in the following chapters. Chapters 2 and 3 describe CDC's epidemiologic and genetic investigations to determine whether the dentist was the source of the infection. Chapter 4 examines CDC's attempts to determine how HIV was transmitted to the dentist's patients.

**Scope and Methodology**

This is the first episode in which a health care worker apparently infected patients with HIV while providing them with medical care. Determining whether the patients contracted the virus from the dentist and, if so, how it was transmitted, posed exceptional research challenges for CDC. We examined CDC's methods and evidence from the inception of its investigation in March 1990 through its research in June 1992. This investigation began when a patient of the dentist was first diagnosed with AIDS but had no admitted risk factors for contracting the disease. CDC's research methods and empirical evidence have evolved substantially and continue to develop, so that the latest research is superior to the initial analyses, and the earliest exploratory work cannot be held to the same standards as the most current. Therefore, in assessing the soundness of CDC's methods and the adequacy of its evidence, we took into account the fact of this progression and the normalcy of such an evolution in scientific explorations.

Numerous studies have now attempted to determine whether other health care workers with HIV have transmitted the virus to patients. We focused our attention on the Florida dentist because he is the first, and thus far only, health care worker who researchers have claimed actually transmitted the virus to patients.⁴

Altogether, eight of the dentist's patients have been identified as HIV-positive. CDC has indicated that five of these eight appear to have

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⁴There was not a single confirmed case of worker-to-patient transmission of HIV among 16,796 patients receiving treatment in 32 different health care settings where an HIV-positive health care worker practiced. Eighty-four of these patients were HIV-positive but had other identified risk factors for the virus. CDC, "Update: Investigations of Patients Who Have Been Treated by HIV-Infected Health-Care Workers," MMWR, 41 (May 15, 1992), 944-46.
Chapter 1
Objectives, Scope, and Methodology

contracted the virus within the dental practice; we pay greater attention to these five individuals than to the three other HIV-positive patients, who apparently were not infected while receiving dental care.

We used the methodologies appropriate for a “critical instance” case study. For the two questions concerning the source and mode of HIV transmission, we collected and examined data from:

1. interviews with federal and state officials, including personnel from CDC and the Florida Department of Health and Rehabilitative Services (HRS);
2. the case files of CDC and HRS;
3. the scientific literature on the epidemiology of bloodborne pathogens; and
4. interviews with other experts on HIV epidemiology.

To answer the evaluation question about the mode of transmission, we examined information on broader issues concerning the transmission of bloodborne pathogens in health care settings. Bloodborne pathogens are disease-causing agents, particularly HIV and the hepatitis B virus, transmitted through blood or other bodily fluids. We included hepatitis in our analysis because HIV and hepatitis are both transmitted by the same means, although hepatitis is far more contagious than HIV. To better understand the means and risks of transmission, we examined evidence concerning infections transmitted to health care workers by patients and vice versa.

We do not refer to the dentist and his patients by name in this report unless they are directly quoted in a public source, even though each of these individuals has been publicly identified by the news media. We typically refer instead to “the dentist” and Patients A, B, C, D, E, F, G, and H to preserve the confidentiality CDC pledged to maintain.

We began data collection in November 1991 and completed it in June 1992. Our work was conducted in accordance with generally accepted government auditing standards.

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*We refer in this report to the hepatitis B virus simply as "hepatitis."
Chapter 2

Did the Dentist Transmit HIV to His Patients? The Patients’ Risk Factors

Did the dentist transmit HIV to some of his patients? CDC’s answer to this question depends on its epidemiologic investigation of the patients, its comparative genetic analyses of the strains of HIV present in the dentist and his patients, and its analysis of the dental practice. The investigation of the patients helped determine whether they could have contracted the virus from sources other than the dentist. The comparative genetic analyses helped resolve whether the strains of HIV present in the patients are the same as those in the dentist (implying that these persons had a common source of infection). The final analysis addressed both whether HIV was transmitted through the dental practice and how these patients might have been infected. In this chapter, we present CDC’s conclusions and begin examining them by assessing the methods used and evidence gained from CDC’s investigation of the infected patients.1

CDC’s Conclusions

CDC states that its investigation “strongly suggests that five patients became infected with HIV while receiving care from a dentist with AIDS.” This conclusion is based on three factors:

- none of the five patients had other confirmed exposures to HIV;
- all five patients had invasive procedures performed by the dentist; and, most importantly,
- all five were infected with HIV strains that were closely related to the strain infecting the dentist but distinct from viruses obtained from control patients living in the same geographic area as the dental practice.

CDC has never stated categorically that the dentist infected his patients. But what does CDC mean by “strongly suggests”? Although CDC does not answer this question directly, it does provide a statistical response based

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2 CDC, “Update,” June 14, 1991, p. 380. The conclusions about the five patients are consistent with, but stronger than, the one reported by CDC after its preliminary inquiry of Patient A. CDC’s initial report noted that “the case reported here is consistent with transmission of HIV to a patient during an invasive dental procedure, although the possibility of another source of infection cannot be entirely excluded.” CDC, “Possible Transmission of Human Immunodeficiency Virus to a Patient During an Invasive Dental Procedure,” MMWR, 39 (July 27, 1990), 491.
on its genetic analyses. These analyses indicate that the probabilities are eight in a million or less that the dentist and five of his patients would have strains of HIV as similar as they do by chance alone. These calculations imply with near certainty that the dentist and these five patients had a common source of infection.

### CDC's Epidemiologic Investigation

The main purpose of CDC's epidemiologic investigation was to determine the risk factors for the dentist's HIV-positive patients. If these individuals had no risk factors outside the dental practice, then the idea that the dentist was the source of infection would be supported. If risk factors for the HIV-positive patients had been identified, however, then the possibility that the dentist was the source would be weakened.

CDC conducted its epidemiologic investigation by attempting to identify the dentist's patients, to discover which ones were HIV-positive, and to learn how these individuals might have contracted the virus. This section describes the basic chronology, methods, and results of this investigation.

CDC becomes involved in epidemiologic investigations only when a state requests CDC's help. CDC typically works in close coordination with a state health department, although at times the work is divided among the agencies. In the case considered here, CDC worked with the Florida HRS. When personnel from both agencies were involved, we refer to "CDC's investigation." When CDC's staff were not directly involved, we refer to HRS.

### Identifying Risk Factors

To determine how individuals contracted HIV, CDC attempts to discover if they have "identified risk factors." Based on its epidemiologic investigations, CDC reports several such risk factors, which differ for males and females.

For males, the risk factors identified most often (percentage of cases as of July 1991 in parentheses) were

1. homosexual or bisexual contact (65);

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3For example, on one test, CDC reported that the probability that the five patients would have genetic patterns so much more similar than a group of other HIV-positive individuals in the area to the dentist by chance alone as .000008 (eight in a million). On another test, CDC stated that the probability by chance alone that Patients A, B, C, E, and G would be more closely related by genetic distance to the dentist than the local controls was .000006 (or six in a million). See chapter 4 for further discussion.

*These risk factors are defined below.
2. intravenous (iv) drug use (19);
3. homosexual or bisexual contact and iv drug use (7);
4. heterosexual contact (2);
   - sex with a person having identified risk (2);
   - sex with an hiv-positive person, risk not specified (0.4);
5. receipt of blood transfusion, blood components, or tissue (2);
6. hemophilia or coagulation disorder (1);
7. other or undetermined (3).

The risk factors most commonly identified for females are different. For females, the most frequently cited risk factors were
1. iv drug use (51);
2. heterosexual contact (33);
   - sex with a person having identified risk (29);
   - sex with an hiv-positive person, risk not specified (4);
3. receipt of blood transfusion, blood components, or tissue (8);
4. other or undetermined (7).

It should be pointed out that the "other or undetermined" category does not necessarily imply that there are additional risk factors that have yet to be discovered. "Other" refers to the few persons who have developed AIDS after exposure to hiv-infected blood within the health care setting. "Undetermined" refers to patients whose mode of exposure to hiv has not yet been identified. This category includes patients under investigation; patients who have died, have been lost to follow-up, or refused interview; and patients whose mode of exposure to hiv remains undetermined after investigation.6

cdc considers these factors to be a hierarchy of risk. in attempting to determine how a person contracted hiv, investigators work down the list.

Once a risk factor has been identified, the investigation typically stops. As a result, if a male admits having had homosexual or bisexual contact, or a female acknowledges IV drug use, additional factors are often not identified. Such a reporting process inherently overstates the relative importance of the risk factors at the top of the hierarchy and understates those at the bottom.

Some risk factors receive little investigation. For example, if an HIV-positive male acknowledges having had homosexual or bisexual contact, or an HIV-positive female admits to IV drug use, or a person concedes having had sexual contact with either homosexual or bisexual IV drug users, this is considered sufficient evidence of how the virus was contracted. Admitting heterosexual contact by itself is not considered adequate evidence of transmission. Heterosexual contact is considered an identified risk factor only if such contacts are identified and determined to be HIV-positive. In other words, CDC would consider an HIV-positive male who acknowledged one homosexual contact as having an identified risk factor but an HIV-positive person with multiple sexual contacts with unknown individuals as having undetermined risk factors.

Determining the risk factors of persons with HIV can pose tremendous challenges to the researcher. Individuals may be reluctant to describe highly personal or illegal activities (such as sexual behavior or drug use) to an agent of the government. They certainly are under no compulsion to do so and may have a variety of motives for concealing or denying the truth.

Information about sexual behavior or drug use is also typically difficult to corroborate. The reasons are partially physical: material evidence of such activities is often fleeting and witnesses rare. The reasons are also partially legal, having to do with protection of individual privacy. For example, the investigators in Florida were not able to ask some direct questions about individual sexual contacts but had to rely on “cluster interviewing.” If Person X claimed to have had sex with Person Y, the investigator could not attempt to corroborate this by asking Person Y, “Have you had sex with Person X?” The researcher instead could only ask Person Y something like “With whom have you had sex?” hoping that Person X would be mentioned.

In addition, it is more difficult to identify and corroborate the risk categories for females than for males. As shown above, the vast majority (95 percent) of male exposures can be traced to conduct (homosexual or
bisexual conduct, IV drug use, receipt of blood transfusions, and so on) of which the male has firsthand knowledge. The researcher can determine the risk factors of males by asking them “Did you have any of these risk factors?” However, a substantial proportion (33 percent) of AIDS cases for females is traced to the conduct of their heterosexual contacts, of which the female may have only secondhand information or even be entirely unaware. For many females, the researcher would need to ask, “Did your partner have any of these risk factors?” This secondhand information is less certain than that obtained firsthand.

A final difficulty regarding this particular investigation cannot be ignored. Any HIV-positive patients of the dentist had a clear financial incentive to claim that the dentist had been the source of the infection so that monetary damages could be claimed. At the very least, potential for financial gain provided incentives for infected patients to deny other risk factors.

In order to determine the risk factors of people with HIV, the researcher must gain the confidence of the subjects so as to acquire accurate and complete information about behavior that puts them at risk of contracting HIV. The investigator must also be diligent at tracking sexual contacts and skillful at cluster interviewing.

**Field Work**

CDC and the Florida HRS jointly conducted the field work. However, most of the field interviews of the patients and their acquaintances were conducted by HRS. The investigators sought to identify risk factors of the infected patients by interviewing them (usually several times) and attempted to corroborate this information by interviewing acquaintances of the patients and collecting other physical information.

CDC initially became involved in this matter when HRS notified CDC that an individual (Patient A) in that state had developed AIDS but had “no identified risks.” Patient A had been diagnosed with AIDS in December 1989. In a routine interview, this individual denied having used IV drugs, having had sexual contacts with HIV-positive persons, or having received blood transfusions; she did indicate that she had received treatment from a dentist whom she suspected of having AIDS. Through follow-up interviews

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6 Three patients had received $1 million settlements from the dentist’s malpractice carrier and additional settlements from the dental care program that provided the dentist’s services.

7 State health departments regularly report to CDC the number of AIDS cases in that state as well as the risk factors of the infected individuals.
and field work, HRS could not identify risk factors for Patient A and so requested CDC to join the investigation.

CDC began its inquiry by interviewing Patient A on March 28, 1990, and the dentist on March 29, 1990. Over the next several months, CDC and HRS attempted to identify risk factors for Patient A through multiple interviews with her, her family, and others who knew her. These attempts did not confirm any exposure to HIV for Patient A other than treatment by the dentist.

During this period, CDC was unable to proceed in its investigation of the dentist's practice. In his initial interview, the dentist indicated that he had retained an attorney who would handle future contact with CDC and HRS; the dentist was not interviewed again. CDC was also prohibited by Florida laws designed to protect patient confidentiality from contacting the dentist's former staff or patients without his consent.

On July 27, 1990, CDC reported that a person had possibly contracted HIV from a dentist, although CDC did not provide any information identifying who the dentist was. On two subsequent occasions, HRS attempted to gain the dentist's consent for contacting his patients and staff. The dentist gave consent on August 24 and wrote an open letter urging his patients to be tested for HIV. The dentist died on September 3. His letter was published by the local newspaper on September 6.

CDC and HRS subsequently took numerous steps to identify and notify the dentist's patients. The dentist had voluntarily provided his remaining records (which included over 100 names) to HRS, although most of the records had been dispersed or discarded since the dentist had sold his practice in July 1989. A local health insurer provided names of individuals it had assigned to the dentist, although it could not verify which individuals had actually used his services. Other local dentists were contacted to see if they had received patient records from this dentist.

Patients were initially notified of their potential risk through the publication of the dentist's open letter in September. The case also received widespread publicity in the local and national press. In November, CDC and HRS sent almost 2,000 registered letters to patients and possible patients who had not yet come in for testing. Eventually, HRS tested about 1,100 patients for HIV; an undetermined number were tested.

*In these interviews, CDC obtained blood samples from both individuals and so was also able to begin the genetic component of the investigation.
privately. It is not known how many patients have chosen not to be tested or to remain unaware that they received treatment from a dentist with AIDS.

Two of the patients (Patients B and C) who came to HRS for testing were found to be HIV-positive. An additional infected patient (Patient D) was identified by HRS through cross-matching a list of dental patients with the Florida AIDS case registry. Three other patients of the dentist (Patients E, G, and H) contacted CDC to report that they were HIV-positive. A former sex partner (Patient F) of one of these individuals was found to be HIV-positive and also a patient of the dentist. Including Patient A, a total of eight patients of the dentist have thus far tested HIV-positive. Because persons with HIV can remain asymptomatic for years, it is possible that additional HIV-positive patients of the dentist remain to be identified.

CDC next attempted to determine the source of HIV transmission to these eight patients. It did this by interviewing these individuals and their acquaintances, families, and health care providers as necessary; by reviewing the patients' medical and dental records; and by testing their sex partners for HIV infection.

CDC reported that three patients (D, F, and H) had behavioral risk factors for HIV. A third patient, Patient C, had unconfirmed risk factors: "The possibility that Patient C had engaged in high risk behaviors was raised during interviews and record reviews; however, behavioral exposures to HIV could not be documented." At the least, Patient C claimed to have had multiple heterosexual partners who could not be identified, located, or tested.

CDC reported that four patients (A, B, E, and G) had no confirmed HIV risk factors. What this means is that CDC was unable to confirm that these patients had been exposed to HIV through IV drug use, sexual contact with homosexual or bisexual men, receipt of contaminated blood products, or sexual contact with individuals having these risk factors. The sexual

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9. In addition, these patients were not linked to the dentist by the genetic studies.

10. Ciesielski et al., p. 800. Patient C was linked to the dentist by the genetic studies.

contacts who were identified were notified and tested; none of these contacts were HIV-positive.12

All eight patients did receive invasive medical procedures from the dentist. These procedures potentially exposed the patients to the dentist’s virus. For at least four of the patients, this potential exposure to HIV was the only exposure confirmed by CDC. Because these procedures possibly explain the mode of transmission, we consider them in greater detail in chapter 4.

Our interviews with CDC and HRS investigators, together with our review of their field notes, indicate that this investigation was thorough and competent. The possibility nonetheless remains that one or more of these patients could have been exposed to HIV outside the dental practice. This possibility is not entirely hypothetical, as gaps remain in CDC’s data. It may be impossible to fill these gaps, however, because the evidence necessary to fill them does not exist or could not be obtained. For example, not all the sexual contacts named by one of the patients could be located and tested.13

CDC found that the evidence “strongly suggests that five patients became infected with HIV while receiving care from a dentist with AIDS.”14 This conclusion was based on CDC’s findings that these patients had no other confirmed exposure to HIV, that each had received invasive dental procedures from a dentist with AIDS, and that the strains of HIV in the patients strongly resembled the dentist’s HIV. Although each finding is important, the absence of confirmed exposure and the presence of invasive dental procedures are theoretically and empirically less compelling than the genetic similarity.

The main theoretical difficulty with the epidemiologic investigation of the patients is that it attempts to “prove the negative.” It is practically impossible to prove that the patients did not contract HIV from a source other than the dentist. The difficulty in proving the negative is further increased in these cases because of the fact that HIV is typically spread

12Patients E and F had been sexual partners, and Patient F had identified behavioral risk factors. Patient E became concerned about Patient F’s behavior and so they were tested for HIV in October 1988; Patient E tested positive and Patient F negative. They had last had sexual contact that autumn. Patient F tested negative again in December 1988 but tested HIV-positive in December 1990.

13This example has been reported in Ciesielski et al., p. 799. We identified other specific examples in our review.

through sexual contact or IV-drug use—behaviors that individuals may be reluctant to discuss and that are difficult to document.

A further weakness of the epidemiologic investigation is that it can show necessary but not sufficient conditions. In other words, it would be necessary to show that the patients did not contract the virus elsewhere to demonstrate that the dentist transmitted HIV to these patients, but showing that the patients did not become infected through identified risk factors is not sufficient to prove that they actually contracted HIV from the dentist.

A couple of examples illustrate these weaknesses. First, many individuals with AIDS do not admit to having risk factors. Through July 1991, there were 12,329 AIDS cases in the United States initially reported as having undetermined risk factors. Even after follow-up information was collected, 491 individuals were still specified as having "no risk identified or other" source of infection. Of these nearly 500 individuals with no identified risk factors, only the five patients of the dentist have been linked to a health care worker. Yet health care workers are not implicated in transmission simply because an individual has no other identified risk factors.

Second, many individuals have received invasive procedures from HIV-positive dentists. In 1990 alone, for instance, HIV-positive dentists in the United States may have conducted over 4 million invasive procedures. The fact that these procedures occurred does not, by itself, imply that any patients were infected.

\[1^{14}\text{CDC, HIV/AIDS Surveillance, p. 16.}\]

\[1^{15}\text{Of the 12,329 individuals, 5,502 were eventually reclassified; 4,708 were under investigation; 1,574 had died, refused interviews, or been lost to follow-up; and 491 were still specified as "no risk identified or other" after follow-up information was collected. Four of the 491 individuals were determined as "other risk factors" after documentation that they had contracted AIDS after exposure to HIV in the health care setting. Of the 487 "no identified risk" cases, 427 responded to a standardized questionnaire. Of these, 138 of 394 responding to questions related to sexually transmitted diseases gave a history of such disease; 96 of 270 interviewed men reported sexual contact with a prostitute. "Some of these persons may represent unreported or unrecognized heterosexual transmission of HIV." CDC, HIV/AIDS Surveillance, p. 16.}\]

\[1^{16}\text{The available data showed 42 surgeons and 156 dental workers with AIDS as of September 30, 1990, and CDC estimated that perhaps 330 HIV-positive surgeons and 1,248 HIV-positive dental workers are practicing in the United States. The estimated number of HIV-infected health care workers was derived by multiplying the number of reported health care workers with AIDS by a factor of eight. CDC, "Estimates of the Risk of Endemic Transmission of Hepatitis B Virus and Human Immunodeficiency Virus to Patients by the Percutaneous Route During Invasive Surgical and Dental Procedures," draft, Atlanta, Georgia, January 30, 1991. The American Dental Association reports unpublished data showing an average of 3,820 invasive procedures per dentist per year. Office of Technology Assessment (OTA), HIV in the Health Care Workplace (Washington, D.C.: November 1991), p. 9. Over 4 million procedures would be performed if 1,200 dentists each performed 3,400 procedures.}\]
In sum, neither the reports of risk factors by patients nor a health care worker's conducting invasive procedures would thus lead necessarily to the conclusion that the dentist was the source of the virus. The genetic study thus carries the heaviest weight as evidence because the sequencing is the only direct evidence that the dentist and the patients carried the same virus.
CDC's field investigation could not demonstrate that the five infected patients had contracted HIV through sexual contact, IV drug use, or other personal activities. All five individuals had undergone invasive procedures performed by a dentist with AIDS, however. These procedures were the only confirmed instances of potential exposure to HIV for these individuals.

To determine whether these five individuals could have been infected with HIV while receiving care from the dentist, CDC studied the genetic characteristics of the HIV in the dentist and his HIV-positive patients. This innovative study has continued to evolve since March 1990, when blood samples were first collected from the dentist and Patient A. This chapter examines CDC's genetic study in several steps. First, we provide a brief overview of the genetic analysis. Next, we discuss the major analytical steps and chronological phases of CDC's genetic analysis. We conclude with a summary.

Overview

AIDS is caused by HIV. The virus contains chromosomes (DNA molecules) that determine what the virus is and what it does. The chromosomes contain the virus's genes, and the genes are composed of nucleotides. Nucleotides consist of chemical components that include "nitrogen bases." It is the sequence of these bases that "constitutes the unique structural and functional individuality of DNA molecules. In fact, the entire genetic language of DNA is contained in the sequence of the nitrogen bases."

HIV mutates over time. A mutation occurs when the sequence of nitrogen bases changes. Because of mutation, the HIV is not identical within every individual but exhibits considerable genetic variability both within and between individuals. Each individual who has HIV, in other words, will have multiple strains of HIV, with each form having a different genetic sequence.

Within an individual, the genetic variation of HIV depends on such factors as duration of infection, the functioning of the immune system, disease

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1The biological functions of DNA include the storage, replication, and transmission of genetic information.

2The nitrogen bases most frequently found in nucleotides include adenine (A), guanine (G), cytosine (C), thymine (T), and uracil (U).

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...stage, and the medical therapy the individual is receiving. Between individuals, the genetic variation also depends on the source of infection. The HIV in persons with a common source of infection (such as sex partners, mothers and their infants, and blood donors and recipients) is more closely related than the HIV in persons without a direct infection link. In general, similarities among strains of HIV are greatest for viruses obtained from a single infected person, intermediate for viruses from persons who have a common source of infection, and least for viruses from persons whose infections are epidemiologically unrelated.

It is possible to assess whether individuals have a common source of HIV infection by determining and comparing the genetic sequences of their viruses. CDC's conclusion that the dentist and his patients had a common source of infection is based on the similarity of the sequences of these individuals and their dissimilarity from other infected individuals.

It is important to understand that genetic sequencing does not and cannot demonstrate that two individuals share the same strain of HIV or that one individual infected another. Genetic sequencing only shows how similar or dissimilar individuals are regarding their HIV. Expert judgment and statistical techniques are necessary to assess whether individuals have a common source of HIV infection.

CDC's Genetic Sequencing Study

CDC's study of the Florida dentist was the first that attempted to determine through genetic sequencing whether individuals had a common source of HIV infection. Previously, scientists had always examined persons with a known common source of infection to see how much genetic variation existed. CDC reversed this process by comparing genetic variation to see if a common source of infection existed. Because CDC was breaking new ground, its study was exploratory and did not always have clear criteria to follow.

We discuss two facets of this study. One concerns the three analytical steps taken by CDC in conducting the study. The other involves the four chronological phases of the study. Each of these analytical steps involves making decisions that can influence the conclusions, and different decisions were made during the different chronological phases. After

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4Chin-Yih Ou et al., "Molecular Epidemiology of HIV Transmission in a Dental Practice," Science, May 22, 1992, p. 1166. Ou gives a number of citations on the effects of duration of infection, host immune pressure, disease stage, and therapy.

5See Ou et al., "Molecular Epidemiology," p. 1166.
briefly describing these steps and phases, we examine the evolution of 
CDC's genetic sequencing study in terms of its analytical steps.

Analytical Steps

Genetic sequencing took place in essentially three steps. First, the 
researchers selected individuals to include in the study and drew blood 
samples from them. This step was taken in Florida by investigators for CDC 
and HRS. Second, researchers extracted and sequenced DNA fragments from 
the blood samples. This step took place primarily in laboratories at CDC 
under the direction of CDC researchers. Third, researchers analyzed these 
sequences to determine their similarity. This final step was taken 
principally by contractors in the computer facilities at Los Alamos 
National Laboratory (LANL) in New Mexico.

Chronological Phases

Although CDC's genetic sequencing study was conducted virtually 
continuously from March 1990 through at least April 1992, four distinct 
stages can be delineated, each of which culminated with a published 
report.

Phase 1 began on March 28, 1990, when CDC collected a blood sample from 
Patient A during its initial interview with her. On July 27, 1990, CDC 
announced that "the laboratory findings in this investigation indicate 
possible transmission of HIV from the dentist to the patient." This ended 
Phase 1.

Phase 2 began on September 6, 1990, when the dentist's open letter to his 
former patients was published, encouraging them to be tested for HIV after 
CDC published its first report. Four other HIV-infected patients (Patients B, 
C, D, and E) were identified in the ensuing months. Phase 2 ended when 
CDC published its laboratory investigation of Patients B, C, and D on 

During Phase 3, which began when Phase 2 ended, CDC identified two 
additional patients (F and G) who were HIV-positive. In this period, the

6CDC, "Possible Transmission of Human Immunodeficiency Virus to a Patient During an Invasive 

7Laboratory work on Patient E had not been completed at the time of publication. CDC, "Update: 
Transmission of HIV Infection During an Invasive Dental Procedure—Florida," MMWR, 40 (January 18, 
1991), 21-27 and 33.
genetic sequencing of Patients E, F, and G was completed. These results were published on June 14, 1991.8

In Phase 4, CDC further refined its genetic investigation of the seven HIV-positive patients, and the results of these efforts were published in an article published in May 1992.9 After this article was prepared, another HIV-positive patient of the dentist (Patient II) was identified. This patient had acknowledged risk factors for infection, and genetic distance measurements indicated that his virus did not closely resemble the dentist's.10 Because Patient H has only recently been identified, and apparently does not have a strain of HIV that is directly related to the dentist's, this chapter does not include his sequencing data.

Step 1: Selecting Individuals and Collecting Blood Samples

In this step, the researchers determined which individuals to include in the study, took blood samples from them, and sent the samples to the laboratory for analysis. The most important decisions that had to be made were

1. Who are the relevant individuals?

2. How should the blood samples be controlled?

The relevant individuals clearly included the dentist and his HIV-positive patients. Identifying the other relevant individuals was not so straightforward. To assess whether the patients might have been infected by the dentist, CDC needed to compare the dentist's strain of HIV with the strains of HIV in his patients and with other HIV-infected individuals (serving as a comparison group). If the patients' strains of HIV were similar to the dentist's and dissimilar from the comparison group, and the strains of HIV for the comparison group were dissimilar to the HIV in the dentist and the patients, this would then suggest that the patients and the dentist had a common source of infection that was different from the sources of infection for the comparison group.11

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9Ou et al., "Molecular Epidemiology," pp. 1166-71.


11CDC designated the members of its comparison group "local controls" (LCs). For consistency in presentation, we have adopted this convention.
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Ideally, either the patients and the LCS would be alike in all relevant characteristics or the characteristics would be randomly distributed across the groups, except with regard to the source of infection, so that differences in HIV could be attributed to differences in the source. The pertinent characteristics of HIV include the factors that affect genetic variation: duration of infection, stage of disease, therapy, functioning of the immune system, and source of infection.

In Phase 1, CDC did not choose a comparison group with the most important relevant characteristics. In particular, none of the group were selected from the area near the dentist's practice. Instead, the comparison group consisted of "17 other distinct North American isolates" for whom sequences currently existed at LANL.

CDC thus could not compare the genetic sequences of the dentist and Patient A to the sequences of similar individuals; it could only compare other dissimilar individuals from the LANL registry. To the extent that there are local population characteristics (for example, where two individuals in an area have similar strains of HIV even if they do not have a common source of infection), failure to include local individuals in the comparison group could have biased the results to show incorrectly that the dentist and Patient A had related cases of HIV even if they did not.

CDC attempted to remedy this deficiency in subsequent phases by collecting samples of blood from HIV-positive individuals at two HIV clinics located within 90 miles of the dental practice. CDC's data collection protocol states that "blood specimens will be collected from all eligible HIV-infected patients who agree to participate during the 30 days following the initiation of the project, or until at least 100 blood specimens are collected." The information collected from the patients included race and ethnicity, mode of exposure, and medical status. Details about the sexual and dental histories of these LCS were not known, because the blood samples were collected anonymously, although most men in these clinics were either homosexual or bisexual or IV-drug users. Unfortunately, no

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12In Phase 4, CDC noted that "no case of a [locally] stable form of HIV has been reported." Ou et al., "Molecular Epidemiology," p. 1107. The possibility of locally stable forms had not been ruled out at the time of Phase I, however.


14The data collection form listed three modes of exposure: male, sex with male; IV drug user; and other or unknown. Current medical status included asymptomatic, symptomatic but not AIDS, and AIDS.

data were collected on the patients' length of infection or type of medical treatment.

CDC analyzed some of the blood specimens it collected. In Phase 2, CDC examined HIV sequences from 8 of the LCS in addition to 21 sequences from the national HIV registry. In Phase 3, CDC included an additional 24 LCS in its analysis. In Phase 4, a total of 35 HIV-positive LCS (including those selected in the earlier phases) were analyzed. Table 3.1 shows the status of the characteristics that can affect HIV variation in the dentist, the patients, and the LCS used in Phase 4, at the time CDC took their blood samples.

Table 3.1 shows that these characteristics were neither identical nor randomly distributed across the patient and comparison groups. Members of the comparison group on the average had probably been infected for a longer period, had a disease that had progressed further, and had received more therapy than the patient group. These systematic differences between the two groups make it more difficult to assess whether the differences in HIV are attributable to the source of infection for the patient group; the HIV strains in the two groups may differ for other reasons. Because the dentist may have more closely resembled the members of the comparison group, however, it might be expected that the dentist's strain of HIV would also differ from those of the patients if he were not the source of infection.

In summary, CDC's use of comparison groups improved substantially between Phase 1, when no LCS were used, and Phase 4, which included 35 LCS. The quality of the comparison groups is weakened because the attributes that can influence HIV variation were neither identical nor randomly distributed among the members of the groups. The effect of this weakness on the conclusions is not known, although it does not appear inherently to bias them toward linking the dentist and the patients. Furthermore, although the use of comparison groups could have been improved, CDC made good faith efforts, given practical constraints, to make sufficient use of experimental comparisons.

Six of the 8 LCS were men and the gender of the 2 others was not known. One of the local controls had been identified as a sexual partner and a patient of the dentist, however. This LC was "occasionally included in the analyses but not in the MMWR articles. [But] it is quite apparent that [his] sequences are not linked to the dentist's sequences nor to any of the other patient's viral sequences." CDC, unpublished data.

CDC is not completely consistent on this point. After noting that 24 new local controls were examined in addition to the original 8, CDC refers to the 31 (not 32) local controls. CDC, "Update," June 14, 1991, p. 379.
Table 3.1: Factors Affecting HIV Variation: Status at Time of Blood Sample Collection

<table>
<thead>
<tr>
<th>Person</th>
<th>Duration of Infection*</th>
<th>Stage of disease</th>
<th>Therapy</th>
<th>Source of Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dentist</td>
<td>More than 3 years</td>
<td>AIDS</td>
<td>AZT</td>
<td>Unknown</td>
</tr>
<tr>
<td>A</td>
<td>Less than 2 years</td>
<td>AIDS</td>
<td>AZT</td>
<td>Dentist</td>
</tr>
<tr>
<td>B</td>
<td>Less than 2 years</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Dentist</td>
</tr>
<tr>
<td>C</td>
<td>Less than 5 years</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Dentist</td>
</tr>
<tr>
<td>D</td>
<td>Unknown</td>
<td>AIDS</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>E</td>
<td>Less than 2 years</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Dentist</td>
</tr>
<tr>
<td>F</td>
<td>Less than 2 years</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Unknown</td>
</tr>
<tr>
<td>G</td>
<td>Less than 2 years</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Dentist</td>
</tr>
<tr>
<td>H</td>
<td>Unknown</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Unknown</td>
</tr>
<tr>
<td>LCs</td>
<td>Unknown</td>
<td>17 AIDS</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*In years, as indicated by CDC's investigation.

The length of time between infection and diagnosis of AIDS can range from 6 months to 7-10 years.

Source: CDC.

Once CDC decided whom to include in the study, it needed to collect blood samples from them and to send the samples to the laboratory for analysis. Two main conditions need to be met if blood samples are to be appropriately labeled and sent from field collection to laboratory analysis.

First, the label must match the sample: blood from individual A must receive label A and blood from individual B label B. Unmatched labeling will produce false analysis. CDC routinely handles blood samples, and we found no reason to believe that these samples were mislabeled.

Second, the labels must be coded to conceal the identity of the patient from the laboratory researchers: the researchers must not know if sample X is from the dentist, a patient, or a control. Identified labeling may produce biased analysis. CDC did not, at least during Phase 1, code labels to conceal the identity of the blood samples. The laboratory researchers...

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One could readily infer from the labels which blood sample was from the dentist and which was from Patient A.
conducting the initial analysis were aware which blood samples belonged to the dentist and which to Patient A. As a result, the potential for perceived or real bias in the analysis existed.

**Step 2: Extracting and Sequencing DNA**

The goal of extraction and sequencing is to correctly identify the genetic information in each individual’s blood. Because the genetic information is not known in advance, it is not possible to determine conclusively that CDC correctly identified these data. However, we can assess whether CDC used methods likely to obtain accurate data. Four methodological questions are important: (1) What genetic information should be examined? (2) Were appropriate techniques used to extract and sequence the genetic information? (3) Were the data examined for contamination? (4) Were the data replicated? This section addresses these questions.

1. What genetic information should be examined? CDC chose to examine portions of the HIV “envelope” gene because it contains the highest amount of sequence diversity among HIV’s structural genes. The genetic diversity is not spread evenly along the envelope gene, however. The sequences of the envelope gene that mutate are called the variable (V) domains; the parts that do not vary are called constant (C) domains. The first variable domain on the envelope region is labeled V1, the next variable domain V2, and so forth; similar designations are used for the constant domains. CDC examined the C2-V3 and V4-C3-V5 regions, although it focused its analysis on the C2-V3 domains because there is enough variation in these domains to distinguish between HIV strains, other studies had analyzed these domains, and the HTV Sequence Database contains a relative abundance of these domains for comparative purposes. CDC examined multiple (5 to 12) sequences from the dentist, the seven HIV-infected patients, and 7 of the LCS. For other members of the comparison group, CDC used a single sequence for each individual.

There is at least some disagreement among experts as to whether CDC examined the portion of the virus most relevant for determining whether the dentist and his patients had a common source of infection. The assumption underlying CDC’s analysis is that if the more variable domains (such as V3) are alike in different individuals, then this would imply that

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aThe envelope gene is a region or segment of the viral genome. (Three regions are known as LTR, gag, and env.)

bCDC is inconsistent in its use of these domains: it uses different domains in different parts of its analysis. Because the reasons for these inconsistencies are not always explained, the reader is left to wonder how they affect the analysis.
the individuals have a common source of infection. Others have suggested that researchers should focus on the more stable domains (such as the C2). If these domains differ across individuals, then this would demonstrate that they have different sources of infection.

2. Were appropriate techniques used to extract and sequence the genetic information? The technique used to extract the genetic information is called polymerase chain reaction (PCR). The first reported use of PCR to extract DNA from HIV was in 1985. PCR is widely used for DNA extraction, and PCR kits are commercially available. Sequencing was also performed with a commercially available kit.

Concerns have been raised about at least one aspect of the genetic extraction and sequencing. For the dentist, the patients, and some of the LCS, DNA was extracted through PCR, 5 to 12 clones of the DNA were produced, and then a sequence was obtained from each clone. In contrast, for the rest of the LCS, one sequence was obtained directly from PCR-amplified DNA. CDC thus essentially had 5 to 12 "samples" of the HIV from some individuals and only one sample from others. This one sample may not be representative of the HIV within an individual: "Direct PCR sequencing is a sampling method that at best generates a sequence composed of the most prevalent base at each position and at worst generates only the sequence of one of the more prevalent viral variants."

3. Were the data examined for contamination? One problem with PCR is possible contamination of the genetic information. CDC reports taking a number of steps to ensure that this did not happen. The laboratory...

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22See, for example, J. Palca, "Trying to Pin Down an Ever-Changing Virus," Science, January 24, 1992, p. 383.

23The laboratory work regarding the dentist, his patients, and the local controls was initially performed at a CDC laboratory under the direction of Dr. Chin-Yi Ou. Dr. A. J. Leigh Brown directed replication of the sequencing on three specimens at the University of Edinburgh, Scotland. These researchers have extensive experience with DNA extraction and sequencing. The PCR technique is described in greater detail in Ou et al., "Molecular Epidemiology," n. 15, p. 1170.


25The Taq Dye Primer Sequencing Kit and the 373A DNA sequencer by Applied Biosystems, Foster City, Calif.


27Smith and Waterman, p. 1156.

28Details are found in Ou et al., "Molecular Epidemiology," p. 1170. CDC's procedures were also reviewed by an outside consultant: J. L. Mullan, unpublished data, July 20, 1990.
facilities CDC used were specifically dedicated to the extraction and sequencing process but had not previously been used for it. Vials and laboratory benches were irradiated to destroy other genetic material that might be present. Chemicals used in the process were measured for a single use. Only one blood sample was processed at a time.

CDC also performed several tests to see whether the genetic information had become contaminated during PCR. These tests essentially consist of dividing each person's blood specimen into two samples and then extracting and sequencing genetic material from each sample. The sequences from each sample were compared with each other as well as with the other specimens. CDC found that the two samples for each person were identical but clearly different from the samples for the other persons.  

4. Were the data replicated? CDC took two steps to replicate the results of the DNA extraction and sequencing. First, the PCR procedure was repeated on a second sample of blood from the dentist and the patients, as noted above. Second, HIV sequences from patients A and B and one control were independently verified by a laboratory not connected with CDC. These steps indicated that the genetic information obtained from the specimens could be replicated.

Step 3: Data Analysis

The genetic extraction and sequencing produced data that showed the arrangement of the genetic material for each DNA sequence for each person. These data were then analyzed to determine their similarity. The main decisions that the researchers needed to make regarding data analysis included (1) What are the appropriate units of analysis? (2) What techniques should be used to determine similarity? (3) What criteria should be used in drawing conclusions from these analyses? CDC's answers to these questions changed substantially during the four phases, as we describe in this section.

1. What are the appropriate units of analysis? Multiple strains of HIV exist in each infected individual. As a result, CDC extracted numerous DNA

Because HIV varies within each person, it is not possible to use HIV sequences to confirm that two blood specimens came from the same person. CDC therefore also sequenced the human leukocyte antigen (HLA), which does not vary within an individual. Comparing these HLA sequences allowed CDC to confirm that two specimens came from the same person.

Of these three individuals, the genetic material for Patient A and the control was extracted by a CDC laboratory that had not previously worked with HIV; Patient B's genetic material was extracted at the University of Edinburgh.
sequences from many of the individuals in the study. For example, CDC determined between 5 and 12 DNA sequences of the dentist, Patients A through G, and some of the LSS. CDC used these data in two ways. The first was to use each individual sequence as the unit of analysis. The second was to create a single "consensus" sequence as a sort of average score for each person.\(^{31}\)

Consensus sequences potentially distort the results. Like any measure of central tendency (such as an average), a consensus sequence discards information about variation—precisely the thing that CDC wanted to evaluate. The size and direction of the potential distortion is unknown, however; it is unclear whether consensus sequences might bias the study toward confirming or toward denying that individuals have similar HIV strains. The primary reason for using consensus sequences is that they simplify data analysis.

CDC was not consistent in its use of individual or consensus sequences in the first three phases of its study. Part of its analysis is based on consensus sequences, part on individual sequences. Since no reasons are given for the choice of consensus versus individual sequences, the question remains whether the choice of sequences affected the results. By Phase 4, virtually the entire analysis was based on individual sequences.\(^{32}\)

2. What techniques should be used to determine similarity? To compare the similarity of the HIV sequences, CDC mainly used three techniques: genetic distance measurements, parsimony cluster analysis, and amino acid signature pattern analysis. In Phase 1, genetic distance measurements were the primary form of analysis.\(^{33}\) Phases 2 and 4 used all three techniques; in Phase 3, the cluster analysis was omitted.

Genetic distance measurements compare the intraperson and interperson variation in nucleotide sequences of HIV. First, each genetic sequence is compared with every other genetic sequence, and the pairwise differences are noted. The variation between two sequences is defined as the

\(^{31}\)A consensus sequence uses at each position the most common nucleotide base among the individual sequences.

\(^{32}\)As noted above, most of the LSS each had only one sequence extracted, and the representativeness of any single sequence is open to question.

\(^{33}\)Genetic distance measurements were not the sole source of analysis in Phase 1. CDC also examined the nucleotide patterns of the dentist and Patient A to determine whether they shared some nucleotide patterns not found elsewhere in the HIV registry. No further explanation of this analysis was provided in the report; interviews with CDC’s personnel indicated that these patterns were recognizable through visual inspection of the data.
percentage of pairs that differ. Intraperson variation is the average difference among all the sequences of one person; interperson variation is the average difference between all the sequences of different individuals.

Parsimony cluster analysis provides information about the relationship of the viruses by creating a statistical “tree” in which the branches represent the strains of HIV within each individual. The HIV strains that most closely resemble each other form adjoining branches. These branches are then connected with the next most similar branch, and so forth, until all branches are attached into a single tree. On this tree, the closer the relationship among HIV strains, the closer the branches: closely related strains thus “cluster” together.

While genetic distance measurements compare overall variation and cluster analysis identifies relationships by using nucleotide sequences, signature analysis attempts to identify unique patterns by comparing arrangements of amino acids. First, the amino acid arrangements of the dentist were compared with those of 32 sequences in the LANL database. If at least 50 percent of the database had a particular amino acid at a particular location but the dentist did not, that specific amino acid of the dentist became part of his “signature.” In all, the dentist’s signature comprised eight noncontiguous amino acids. Second, the dentist’s amino acid sequences were compared with those of his patients and the LCS to determine the similarity of the dentist’s signature with these other individuals.

CDC considered whether genetic distance measurements, parsimony cluster analysis, and amino acid signatures were independent tests of similarity by computing the correlations between them. CDC found little correlation between the distance measurements and the amino acid signatures and so concluded that they were independent tests. Distance measurements and cluster analysis, in contrast, appear to be closely related techniques; for example, they are based on the same data. These two techniques provide differing ways to view the same evidence.

3. What criteria should be used in drawing conclusions from these analyses? CDC used ad hoc criteria through all four phases of the study, although the statistical standards improved steadily. The main reason that CDC could not explicitly specify its criteria is that it did not have the statistical information necessary for determining these criteria.
In Phase 1, CDC's conclusions were based on genetic distance measurements from the consensus sequences of the dentist, Patient A, and a comparison group of 17 HIV strains from the national HIV registry. These genetic distance measurements over the V3-V4-C3-V6 domains showed the following results:

- The dentist and Patient A differed by 1.2 percent.
- The dentist and the 17 individuals in the comparison group differed by an average of 8.1 percent (range: 5.1 to 10.2 percent).
- Patient A and the individuals in the comparison group differed by an average of 8.8 percent (range: 4.7 to 12.9 percent).
- The individuals in the comparison group differed by an average of 9.2 percent (range: 4.7 to 12.9 percent).
- The average difference (4.0 percent) between the individual sequences of the dentist and Patient A was similar to the average differences (between 3.4 and 5.8 percent) between individuals in the HIV registry known to have a common source of infection.34

Based on the "high degree of similarity between the HIV strains infecting the patient and the dentist," CDC concluded that

"The case reported here is consistent with transmission of HIV to a patient during an invasive dental procedure, although the possibility of another source of infection cannot be entirely excluded. . . . The epidemiologic and laboratory findings in this investigation indicate possible transmission of HIV from the dentist to the patient."35

CDC recognized that this conclusion was highly tentative. Because little was known about the intraperson and interperson variation in HIV, no settled criteria could be used to determine whether individuals had a common source of infection.36 Because HIV sequences vary within every person and no two individuals have the exact same sequences, the HIV sequences within all infected persons are more or less alike. The question that CDC could not firmly answer is, How similar must the HIV sequences within two individuals be in order to conclude that the individuals have a common source of infection? As CDC notes, "The quantitative criteria for determining epidemiologic linkage based on HIV sequences are just now

34These linked individuals included two instances of sexual transmission, one of perinatal transmission, and one in which a group of persons with hemophilia became infected from a single batch of contaminated blood.


being developed." CDC thus relied heavily on the experience of its analysts rather than on established standards in deriving its conclusion.37

CDC's decision to release its initial report of Phase I has been highly controversial. A main criticism of the report is that it was unduly alarmist because CDC knew neither that the dentist had infected the patient nor how the infection had occurred. From this perspective, CDC acted precipitously because the report frightened the public without providing either definitive evidence supporting the conclusions or recommendations on what to do about them.

An alternative view is that CDC acted appropriately by publishing this report. The main reason supporting this idea is that the purpose of MMWR is to disseminate "provisional" "accounts of interesting cases, outbreaks . . . or other public health problems of current interest to health officials." By these standards, this report was suitable for publication. Furthermore, CDC explicitly noted the provisional nature of the report at several points.

CDC recognizes the tension that exists between releasing information too soon (when the probabilities are higher that the conclusions will eventually be disproved) and too late (when it will appear that CDC is withholding information affecting public health). Determining the "right" time to release public health information is a matter of professional judgment. In this case, CDC decided to risk erring on the side of releasing the information too soon.

In Phase 2, genetic distance measurements showed that the HIV in the V4-C3-V5 regions of the dentist and Patients A, B, and C differed by an average of 1.8 percent, whereas the average distance of their viruses from the 8 LCS was 4.8 percent. Genetic distance measurements also indicated that the V3 region of the dentist and Patients A, B, and C differed by an average of 3.4 percent, whereas the average difference of these individuals from 7 of the LCS and 21 other LANL sequences was approximately 13 percent. CDC calculated that there was a 0.006 probability that the HIV sequences from Patients A, B, and C would be closer by chance alone to

36CDC's conclusions, it should also be remembered, are not based solely on DNA sequences. Its epidemiologic investigation did not identify any other sources of infection for Patient A.

38Statement of purpose on the editorial page of MMWR.

39The HIV from one of the local controls (the one who had been a sexual partner and patient of the dentist) was not closely related to the strain present in the dentist. Data from this person were not reported because the analysts were uncertain about how to interpret them. Interview with analyst, January 29, 1992.
Chapter 8
Did the Dentist Transmit HIV to His Patients? The Genetic Analysis

The sequence from the dentist than to the sequences of the 8 controls.\footnote{CDC used a Wilcoxon rank-sum statistic to measure the probability that patients A, B, and C would be closer by chance alone to the sequence from the dentist than to the sequences of the 8 controls.} The cluster analysis indicated that the viruses of the dentist and patients A, B, and C were more closely related to each other than to the virus in the other individuals in the study. CDC also reported that its examination of the amino acids indicated that the dentist and Patients A, B, and C shared a unique signature pattern absent from the HIV of the others in the comparison group. From this analysis, CDC concluded that its evidence "strongly suggests that at least three patients of a dentist with AIDS were infected with HIV during their dental care. . . . DNA sequence analyses of the HIV strains from these three patients indicate a high degree of similarity of these strains to each other and to the strain that had infected the dentist—a finding consistent with previous instances in which cases have been linked epidemiologically."\footnote{CDC, "Update," January 18, 1991, p. 26.}

In Phase 3, CDC included the results for Patients E, F, and G. CDC found that the V3 region of Patients E and G differed from those of the dentist by an average 2.5 and 4.6 percent and differed from the 31 LCSs by an average of 9.4 and 11.2 percent, respectively. Patients E and G also had the same amino acid signature pattern as the dentist. Patient F’s V3 region differed by an average of 0.2 percent from the dentist’s and did not have the same signature pattern.

CDC expanded its earlier conclusions by stating that its "investigation strongly suggests that five patients (patients A, B, C, E, and G) became infected with HIV while receiving care from a dentist with AIDS."\footnote{CDC, "Update." June 14, 1991, p. 380.} CDC also concluded that patient F did not appear to have been infected through the dental practice. CDC did not provide any additional statistical information about the probability that these conclusions were correct.

Phase 4 yielded the most detailed analyses. The results of the genetic distance measurements are shown in table 3.2.
Table 3.2: Genetic Distance Measurements*  

<table>
<thead>
<tr>
<th>Person</th>
<th>Average Intraperson variation</th>
<th>Average Interperson variation between:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dentist</td>
<td>LC</td>
</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>2.0 (0.0-4.5)</td>
<td>3.4 (0.8-6.2)</td>
</tr>
<tr>
<td>B</td>
<td>1.9 (0.4-3.7)</td>
<td>4.4 (2.1-7.0)</td>
</tr>
<tr>
<td>C</td>
<td>1.2 (0.4-1.6)</td>
<td>3.4 (2.1-4.9)</td>
</tr>
<tr>
<td>E</td>
<td>2.1 (0.4-3.7)</td>
<td>3.4 (1.2-6.6)</td>
</tr>
<tr>
<td>G</td>
<td>2.8 (1.6-3.7)</td>
<td>4.9 (2.9-7.0)</td>
</tr>
<tr>
<td>D</td>
<td>7.5 (0-9.9)</td>
<td>13.6 (11.5-15.6)</td>
</tr>
<tr>
<td>F</td>
<td>3.0 (0.8-5.8)</td>
<td>10.7 (8.2-13.6)</td>
</tr>
<tr>
<td>A,B,C,E,G</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D,F</td>
<td>c</td>
<td>12.2</td>
</tr>
<tr>
<td>LCb</td>
<td>c</td>
<td>11.0</td>
</tr>
</tbody>
</table>

Table 3.2 shows that the average genetic distance from Patients A, B, C, E, and G to the dentist was much smaller (4.0 percent) than the average distance from the dentist and these patients to the LCS (11.0 and 11.2 percent, respectively). In addition, the average genetic distance from Patients D and F to the dentist and the LCS was 12.2 percent and the average distance among the LCS was 12.0 percent. This suggests that the HIV strains in Patients A, B, C, E, G and the dentist were more closely related to each other than to the other individuals, that Patients D and F were less closely related to the dentist, and that the others were less closely related to each other. CDC reports that the probability by chance alone that Patients A, B, C, E, and G would be more closely related by
genetic distance to the dentist than the LCS was .000006 (or six in a million).  

Parsimony cluster analysis was used to produce numerous trees showing the relationship among the viral strains in the dentist, the seven patients, and the LCS. In each of these trees, the genetic sequences of the dentist and patients A, B, C, E, and G clustered together, according to the authors. Although the cluster analysis does not provide statistical tests, its results are consistent with the genetic distance measurements.

The results of the amino acid signature pattern analysis in Phase 4 are shown in tables 3.3 and 3.4. In each cell of this table, the values range from .0, where there is no correspondence among the amino acids in the signature patterns, to 1.0, where the signature patterns are identical.

| Table 3.3: Frequencies of Amino Acids in the Signature Patterns of the Reference Group* |
|---------------------------------|---|---|---|---|---|---|---|---|---|
| Frequency in:                  | E  | T  | E  | S  | T  | A  | I  | Q  |
| Reference                      | .63| .81| .69| .59| .69| .66| .72| .56|
| Florida LCSs                   | .67| .67| .63| .75| .42| .60| .84| .45|
| Dentist                        | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| A,B,C,E,G                      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| D,F                            | .55| 1.0| .73| .91| 0  | .45| .82| .82|

*The reference set is composed of 32 distinct V3 region sequences available from the LANL HIV Sequence Database. The letters in the column heads specify the amino acids that comprise the signature pattern.


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53*This is the probability level of the Wilcoxon rank-sum statistic. This statistic is a conservative way to test for similarity. CDC notes that genetic distance measurements using the available V4-C3-V5 sequences also support this analysis. Ou et al., "Molecular Epidemiology," p. 1167.

44*The various data permutations CDC considered are described in Ou et al., "Molecular Epidemiology," pp. 1167-68.

45*For additional detail, see Ou et al., "Molecular Epidemiology," pp. 1168-69.
The results of the genetic distance measurements and cluster analysis are also supported by the amino acid signature pattern analysis. Tables 3.3 and 3.4 demonstrate that the signature pattern of the dentist was matched almost exactly by Patients A, B, C, E, and G while Patients D and F as well as the LCS had distinctly different patterns. CDC reports that the probability that the five patients would have patterns so much more similar than the LCS to the dentist by chance alone as .000008 (eight in a million). In making this estimate, Ou reports that

"In computing the statistical significance of these findings, we used the sequences from those individual clones for each of the patients A, B, C, E, and G that agreed least with the dentist's signature. For the seven LC cases in which there were multiple clones, we used the clone sequence that agreed best with the dentist's signature. This biased the outcome toward the hypothesis that the viruses of the dental patients and the LCS were equally similar to the dentist's viruses."^46

 CDC concluded on the basis of its genetic analysis that the evidence "strongly suggests" that five patients became infected with HIV while receiving dental care from the dentist with AIDS. We concur that CDC's evidence supports this conclusion. It is nonetheless possible, although highly unlikely, that the dentist was not the source of infection.

CDC's innovative analysis appears generally to have been performed competently. Although CDC at times lacked clear criteria to use in making its research decisions, these decisions look sensible. The most obvious mistake that CDC made in its genetic analysis was to label the blood

^46Ou et al., "Molecular Epidemiology," p. 1168.
samples in such a way that researchers knew which sample belonged to
the dentist and which to Patient A. As a result, the potential for bias—real
or perceived—in the analysis existed.

Prior to this investigation, CDC had suggested that the transmission of HIV
from health care workers to patients would occur "only very rarely, if at
all." The epidemiologic and genetic examination of the Florida dentist and
five of his patients apparently demonstrated that such transmission was
more than a theoretical possibility. Yet other studies of over 15,000
patients treated by HIV-positive health care workers have thus far failed to
demonstrate even one additional worker-to-patient transmission. As a
consequence, the public policy implications of this one outbreak of HIV in a
health care setting are unclear.
CDC's epidemiologic study found that none of the five patients had confirmed exposure to HIV but that they had received treatment from the dentist with AIDS. The genetic analyses indicated that these five patients were infected with HIV strains that were closely related to each other and the strain infecting the dentist but distinct from viruses obtained from control patients living in the same geographic area as the dental practice. But if the evidence suggested that the dentist was the source of infection, the question remained: How had HIV been transmitted to the patients?

CDC's answer to this question was based on its investigation of the dental practice. CDC investigated three potential modes of HIV transmission: (1) sexual contact with the dentist, (2) contact with contaminated equipment, and (3) direct contact with the dentist's blood. CDC also attempted to determine whether the transmission was accidental or intentional.

CDC has not been able to identify precisely the manner by which the virus was transmitted to the five patients on the basis of its investigations. The weight of evidence nonetheless suggests that the patients contracted HIV through accidental, direct contact with the dentist's blood.

In this chapter, we examine each of the four potential modes of transmission, the methods CDC used to gather evidence, and the evidence that CDC gathered.

**Investigation of the Dental Practice**

The dentist used his office from 1981 until July 1989, when he stopped practicing and sold the office to another dentist.\(^1\) When the dentist closed the practice, he dispersed most of the patients' records to other practitioners and threw out most office records such as appointment books.\(^2\) His dental staff left the clinic.\(^3\) Most of the dental equipment was sold, and the office was remodeled. To determine who infected the dentist's patients and how they were infected, CDC therefore had to collect and analyze information from the dentist, his patients, staff, and office

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\(^1\)The dentist maintained a solo practice except between September 1985 and February 1986, when he had an associate.

\(^2\)The dentist apparently kept only the records of patients who owed him money.

\(^3\)One staff member stayed with the clinic for a period.
How Was HIV Transmitted to the Patients?
The Dental Practice

Chapter 4
after his practice was closed. In this section, we review CDC's data collection efforts. 4

The Dentist

Investigators from CDC and HRS first interviewed the dentist on March 29, 1990, at his home. The meeting appears to have been brief. During the interview, the dentist indicated that he had retained an attorney who would handle future contacts with CDC and HRS. The investigators took blood samples from the dentist at the conclusion of this interview. CDC's one-page written summary of this interview contains a brief description of the dentist and his dental practice, including his infection control practices.

Representatives from HRS did meet with the dentist on two other occasions. Both times, the dentist's attorney was present. The purpose of these meetings was to persuade the dentist to announce to his patients that they should be tested for HIV. To gain cooperation from the dentist, and to avoid conflict with his attorney, no real effort was made to collect additional information from the dentist at these meetings. 6 The dentist died shortly after he gave consent for contacting his former patients.

CDC did not bring a dental expert to its first, and only substantive, interview with the dentist. More detailed information about the dentist's practice (in particular his infection control practices and self injuries) might have been collected if such an expert had been present. Because this was the only interview CDC investigators held with the dentist, this oversight was particularly unfortunate. CDC recognizes that it was a mistake not to have included a dental authority in the interview and has since indicated that appropriate experts would be used if similar cases arise in the future. 6

To understand CDC's error in this matter, it may be helpful to recall the circumstances surrounding the investigation. First, Patient A was one of many AIDS cases with no identified risk factors. Through July 1991, there were over 12,000 AIDS cases in the United States initially reported as having

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5The CDC and HRS personnel who attended these meetings neither took notes nor wrote summaries of them.

6In addition, CDC has developed a standard questionnaire to administer to health care workers implicated in HIV transmission.
undetermined risk factors; several thousand of these were being investigated. Second, efforts to determine risk factors for Patient A involved numerous interviews with numerous acquaintances. Third, no health care worker had yet been implicated in the transmission of HIV in a health care setting. At the time of the meeting with the dentist, the source of infection for Patient A remained an open question, and the dentist was one of many leads that CDC was pursuing. Given these three factors, it is unfortunate, but perhaps not surprising, that greater attention was not given to obtaining information from the dentist.

The Patients

CDC had to reconstruct a list of the dentist's patients because the dentist had dispersed or discarded most of his records. Over 1,000 patients eventually were interviewed briefly as part of the counseling they received before or after they were tested for HIV. These interviews included questions about the dentist's practice, including the quality of his care and perceptions of his mental state.

CDC and HRS conducted more thorough interviews with the eight HIV-positive patients as they were identified. These patients were asked to describe the dental treatment they received. These interviews, it is worth noting, directed the patients to recall the details of normally ordinary dental procedures 1 or more years after they happened.

The Dental Staff

All 16 of the individuals who worked on the dentist's staff between 1981 and 1990 were identified, contacted, and interviewed twice. HRS interviewed all these staff members individually. Follow-up interviews were later conducted by CDC and HRS. Several were interviewed a third time as a group.

The Dental Practice

CDC and HRS inspected the dentist's practice, even though it had been sold, the office remodeled, and much of the equipment replaced. CDC and HRS

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8 As HRS did not document these interviews, this information is based on our interviews with HRS officials.
9 These individuals were also tested for HIV; all tested negative.
10 Only one individual, who worked for the dentist for a short time, was not interviewed twice.
were able to locate and examine some of the dental equipment. A small group of dental staff members gave CDC and HRS investigators a tour of the office and described office procedures, including infection control practices.

Potential Modes of Transmission

One main purpose of these interviews and inspections was to determine how the virus was transmitted to the patients. In this section, we examine the evidence concerning the potential modes of transmission: sexual contact, contaminated dental equipment, or direct contact with the dentist's blood.

Sexual Contact

There is no evidence to suggest that the patients contracted HIV through sexual contact with the dentist, and strong evidence exists that sexual contact with the dentist was not the mode of transmission. All the infected patients denied that they had had sexual contact with the dentist. CDC's interviews with these patients and the dental assistants also indicated that the dentist had never used general anesthesia on any of these patients, so some hypothetical sexual contact with an unconscious patient is not plausible.

Contaminated Equipment

It appears unlikely for five general and specific reasons that the HIV was transmitted through contaminated dental equipment. The evidence is far from ironclad on this matter, however.

First, HIV is not easily spread except through direct contact with blood or semen. The length of time that the virus will remain infectious outside the body depends on the quantity of the virus and the environmental conditions. The quantity of HIV likely to be present on dental equipment, and the environment in a dental practice, does not produce favorable conditions for lengthy survival of HIV.

The investigators examined numerous potential modes of transmission. For example, the staff indicated that the dentist occasionally did not change gloves between patients but simply washed them. An unlabeled canister of soap was found in the office. The investigators theorized that the dentist may have used this soap to wash his latex gloves, that the soap may have caused the gloves to deteriorate, and that the virus was transmitted through these (now flawed) gloves. Because tests showed that the soap did not cause the latex to disintegrate, this possibility was eliminated from consideration.

The larger the quantity, and the more favorable the conditions, the longer the infectiousness. CDC, "Recommendations," MMWR, 36, No. 25 (August 21, 1987), 106.
Despite the fact that HIV does not typically survive long outside the body, however, it is nonetheless possible that HIV-contaminated dental equipment could transmit the virus for short periods if the equipment were not properly cleaned.

Second, HIV is killed by ordinary disinfection or sterilization, and the dental staff claimed to use a number of such infection control practices. Surgical instruments were routinely heat sterilized ("autoclaved") by 1987. Most other instruments were normally heat sterilized or soaked in a sterilizing solution between patients. Some equipment (such as prophylaxis angles, the "picks" hygienists use to clean teeth) was typically wiped with alcohol between patients. Only disposable anesthetic needles were used after 1983, and the staff reported no instances of reusing needles on different patients. A single needle was sometimes used several times on a single patient, however.

While the staff claimed to use infection control practices as a matter of routine, it is difficult to verify their statements or to determine how often breaches in infection control actually occurred. The office had no written infection control protocols, procedures for training staff in these protocols, or policies for maintaining and documenting them. Although it appears that the infection control practices of the office improved over time, it is also clear that the staff did not always follow "universal precautions" as specified in CDC's 1987 recommendations for preventing transmission of HIV in the health care workplace.

The statements of dental staff should be viewed critically in the absence of supporting evidence. Because the dental staff had primary responsibility for maintaining infection control practices, disclosing breakdowns in these practices could put the staff in professional, financial, or legal peril.

Third, there were no outbreaks of other infectious diseases (such as hepatitis) in the dental practice. Such outbreaks would have provided evidence that the dentist's infection control practices were inferior. The absence of infectious outbreaks does not demonstrate that infection control practices were superior, however.

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13 This section is based on our review of CDC's interviews with the dentist's staff.

14 The dentist's autoclave (heat sterilizer) was found and tested; it worked properly.

15 For example, the dentist's staff did not flush out handpieces after each use as recommended. See CDC, "Recommendations," p. 78. The extension of blood and bodily fluid precautions to all patients regardless of the bloodborne infection status is referred to as "universal precautions."
Fourth, the infected dental patients received different treatments, on different days, over an extended time. The five patients made 48 documented visits to the dental office between November 1987 and June 1989. On four occasions, two of the five infected patients visited the dentist on the same day. The probability of this happening by chance alone is 60 percent; in other words, there is nothing unusual about this number of shared visits.

On the days of shared visits, furthermore, different procedures were performed using different instruments. When Patients A and B both had appointments on December 17, 1987, Patient A had teeth extracted and Patient B received an examination for a toothache. On July 11, 1988, Patient B had periodontal scaling and an extraction; Patient E received a crown. These procedures probably called for different instruments. It is not clear whether Patient E received a local anesthetic, although Patient B certainly did. When these persons again had appointments on August 29, 1988, Patient B had a bridge placed and Patient E had restorations on two molars. Both patients probably received local anesthetic, but the other instruments used would have been different for each person. Patients B and C both had tooth cleanings on January 20, 1989, and neither person apparently received local anesthetic. The dental hygienist cleaned Patient B's teeth; it is not known who cleaned Patient C's teeth.

Fifth, the patients' strains of HIV more closely resembled those of the dentist than of each other. This pattern would not be expected if the virus was spread from patient to patient through contaminated equipment. The possibility that the dental equipment was contaminated by the dentist himself can also be discounted. According to dental staff interviews conducted by CDC, only once since 1987 did the dentist's hygienist clean his teeth, and the dentist neither received other treatment within the office nor treated himself. It thus appears highly unlikely that the HIV was transmitted to the patients through contaminated dental equipment.

16Patient C is the only one of these patients who had received treatment prior to November 1987. Patient C's treatments began in 1986. Patient B had the most (21) appointments and Patient G the least (2).


18CDC calculated this probability by assuming that patient visits occurred randomly on the days the dentist's office was open between the days of the first and last appointments of the patients and that no patient visited the dentist twice on a single day.

19Once or twice, the dentist had his hygienist dab medication on his mouth with a cotton-tipped swab, which was then discarded.
Direct Contact With the Dentist's Blood

It seems likely that the patients were infected through direct exposure to the dentist's blood after the dentist injured himself. However, the evidence supporting this assessment is largely indirect.

Three pieces of indirect evidence are most important. First, health care workers do occasionally injure themselves while performing medical procedures. Second, these injuries sometimes come into contact with a patient's wounds, exposing the patient's blood to the worker's blood. Third, these exposures have led to infections. This evidence suggests that it is possible for the dentist to have transmitted HIV to his patients through dental procedures.

The likelihood of spreading HIV through medical procedures depends on this joint probability of an HIV-positive health care worker having a self-inflicted injury, having an injury that exposes the patient's blood to the worker's blood, and having an exposure that leads to infection. CDC has estimated that there is between a .00038-percent (1 in 263,000) and .000038-percent (1 in 2,630,000) probability that an individual patient undergoing an invasive dental procedure by an HIV-positive dentist will be infected with HIV.1 These odds are based on the assumptions that a dentist has a 0.4-percent chance of self-injury during a procedure, a 32-percent chance of contacting the patient's wound with this injury, and a chance of HIV infection after this exposure of between 0.03 percent and 0.3 percent.2 According to this risk-assessment model, the odds of a single dentist infecting five patients within 2 years would be infinitesimally small.

This model may or may not accurately describe the overall risk of contracting HIV from an HIV-positive dentist, but even if it is generally correct, it does not necessarily describe the riskiness of any individual practice. Individual dentists can vary in their injury, contact, and infection rates. A dentist who suffers more frequent injuries, has higher contact rates, or is more infectious could produce significantly higher infection risks. As a result, even though it appears to be theoretically almost

---


22The upper bound, 0.3 percent, was taken from estimates of the risk of HIV transmission from patient to health care worker from a single needlestick by an HIV-infected needle. The lower bound, 0.03 percent, was arbitrarily chosen as a reduction by a factor of 10.

23In a survey of self-reported injuries of 89 dentists, 32 percent reported 2 or more injuries per month and 3 percent indicated more than 15 injuries per month. See Ciesielski et al., "Transmission," p. 803, for citations.
impossible for one dentist to infect five patients, the actual probability depends on the specific injury rates, contact rates, and infectiousness of the particular dentist.

**Injury Rates**

CDC does not know how often the dentist injured himself. Dentists are not required to maintain injury logs, and this dentist kept no such records. The dentist did indicate during his interview with CDC that he did not remember ever suffering a severe cut during a dental procedure. He acknowledged that he occasionally stuck himself while recapping the needles used to administer anesthetic, although his assistant would usually recap these needles. No patient could recall the dentist cutting himself (by a needle or other sharp tool) or any exposure to the dentist’s blood, although one patient suggested that the dentist might have injured himself on two occasions while he was providing treatment.24

The dentist did at least have several chances to injure himself while treating these patients. For example, all these patients received several injections of local anesthetic. The dentist could have injured himself during these injections without the patients’ awareness. The dentist may also have been at greater risk of injuring himself if he suffered from peripheral neuropathy (temporary loss of control or trembling in the hands). Although it has not been documented that the dentist had such a condition while practicing, between 0 and 36 percent of persons with AIDS have experienced this malady.25

**Contact Rates**

It is not possible to estimate the contact rates because the dentist’s injury rate is unknown. The dentist routinely wore gloves after 1987, and gloves can serve as a barrier between the bodily fluids of dentists and their patients. Gloves do not prevent most injuries caused by sharp objects, however, and so do not necessarily reduce contact rates.

**Infectiousness**

It is not known whether the dentist was unusually contagious during the period the infections are believed to have occurred. No evidence indicates that the dentist had a particularly virulent strain of HIV, and there is some evidence that he did not. If the virus had qualities that made it especially infectious, one would expect that the five infected patients would have

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24Patient B did remember cutting her own tongue on a tooth that had been sharpened in the course of treatment, although she did not know whether the dentist had also cut himself on this tooth. Patient B also recalled another occasion in which the dentist struggled with a tooth extraction, possibly injuring himself.

How Was HIV Transmitted to the Patients?
The Dental Practice

also spread the disease to their sexual partners. This did not happen. The infected patients did not infect any of their sexual partners.

It is possible that the dentist had relatively high quantities, or "titer levels," of HIV in his blood at the time the infections occurred and that this high titer level increased the possibility of infection, however. Although the relationship between HIV titer levels and infectiousness has not been proven, research has shown that higher titer levels of hepatitis are associated with greater infectiousness.

There are a couple of reasons to believe that the dentist did have higher titer levels while he was treating patients who became infected. All five of the patients received treatment "after the dentist was diagnosed with AIDS and had evidence of severe immunosuppression . . . [which is] associated with higher viral titers." At least two patients also received invasive procedures during a brief period when the dentist had discontinued AZT (zidovudine) treatments. During this period, the dentist's titer may have increased. In March 1992, CDC was measuring the titer of the dentist's blood sample taken in March 1990. However, the relationship is unclear between this titer level and that of the dentist between 1987 and 1989, when it is thought that the patients were infected.

Intentional Transmission

No good evidence suggests that the dentist deliberately infected his patients. Substantial evidence exists that he did not. The dentist agreed to be interviewed by CDC and to have a blood sample taken for genetic sequencing. He wrote an open letter to his patients encouraging them to be tested for HIV. In this letter, written shortly before his death, the dentist stated that "I am a gentle man, and I would never intentionally expose anyone to this disease. I have cared for people all my life, and to infect anyone with this disease would be contrary to everything I have stood for."

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26 Patient E and Patient F had sexual contact, but it appears that they did not infect each other. As mentioned earlier, CDC was not able to identify all the sexual contacts of at least one of the patients.

27 CDC, "Recommendations," p. 3.


29 After his first meeting with CDC, he refrained from interviews on advice of his counsel. This was not unusual. The infected patients also retained legal counsel.

His family, staff, health care providers, patients, and other acquaintances also suggested in interviews that there was no indication that the dentist had intentionally transmitted HIV to his patients. In addition, all the infected patients were awake while they received dental treatment, and staff were usually present, yet neither patients nor staff noted or suspected unusual behavior by the dentist. Because the personnel at CDC and HRS are health investigators, not criminal investigators, they brought this matter to the attention of the attorney general in Florida, but that office declined to become formally involved, noting the absence of supporting evidence.

One individual, an acquaintance of the dentist, has claimed in a deposition that the dentist may have been inclined to infect his patients in order to bring attention to the disease. This deposition was forwarded to the Florida HRS, and HRS personnel then also interviewed this individual. HRS in turn delivered the information to the Florida attorney general’s office. Both offices determined that no additional action was warranted.

CDC examined three ways that the dentist potentially transmitted HIV to five of his patients:

- sexual contact with the dentist,
- contact with contaminated equipment, and
- direct contact with the dentist’s blood.

CDC also attempted to determine whether the dentist accidentally or intentionally infected these patients. CDC’s investigation involved interviews with the dentist, his patients, and his dental staff, among others, and an examination of his office.

CDC could not identify on the basis of its investigation exactly how HIV was transmitted to the five patients. The weight of evidence nonetheless suggests that the patients contracted HIV through accidental, direct contact with the dentist’s blood.

Because CDC was unable to determine precisely how the virus was transmitted, the case of the Florida dentist provides little specific information about how to prevent such occurrences in the future. In particular, the investigation of the dental practice failed to show that certain medical procedures are riskier than others in terms of HIV transmission.
Appendix I

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