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## HIV Antibody Testing: Performance and Counseling Issues

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# HIV Antibody Testing:

# Performance and Counseling Issues

*Michael Gross, Ph.D.*

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*This article assesses the performance of currently used tests for exposure to human immunodeficiency virus (HIV), the infectious agent associated with acquired immunodeficiency syndrome (AIDS); suggests, in view of that information, guidelines for counseling people seeking HIV antibody testing; and evaluates the claim that because antibody test results will effect behavior change in those who are infected, all members of high-risk groups should be tested.*

*HIV testing is likely to yield a high proportion of false-positive results in low-risk populations and infants born to infected mothers. A negative result may not establish freedom from infection in high-risk groups or the offspring of infected mothers. Counseling should relate these generalizations to a client's motivation for and expectations from testing. In evaluating a client's risk of exposure, past and present, counseling should provide both information about and reinforcement for behavioral risk reduction.*

*The assertion that members of high-risk groups ought to learn their antibody status is questioned in view of concerns about test performance and even more serious questions about the psychological impact of test results — both short- and long-term — on people's adaptation to protective sex and modification of drug use patterns.*

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In November 1983 — not long after scientists had concluded that AIDS was caused by a transmissible agent and months before the disease was definitively associated with a new virus — the New York Academy of Medicine published a comprehensive summary of the state of knowledge about the syndrome. In the book's more than six hundred pages, containing dozens of papers about AIDS, just three index entries on blood screening refer to two short papers attempting to measure the efficacy of requesting that prospective donors who are at risk defer themselves. In current AIDS compendia, in contrast, techniques, applications, and interpretations of testing occupy whole chapters.

From a technical interest — how best to screen donations of blood and tissue for the agent associated with AIDS — testing has evolved into a major area of biomedical research and an even larger preoccupation, sometimes a battleground, of public policy.

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Should some or all citizens be subjected to mandatory testing? Is testing appropriate for purposes of insurance underwriting? Is testing a productive adjunct to risk-reduction education and counseling efforts? Are there any occupations for which screening is necessary to prevent transmission in the workplace? Are there valid reasons for testing institutionalized populations?

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## Test Methods and Performance

An important consideration in determining valid uses of testing is the performance of currently available methods. This section, therefore, examines the methods, accuracy, and efficacy of current procedures and the possible meanings of test results. The next section considers the implications of that information in an individual's decision about whether to elect for HIV testing, and in relation to his or her adherence to risk-reduction guidelines. Some of the patterns of response by individuals to their test results are then described as a context for a discussion in the following section of principles that ought to underly the adoption of testing programs.<sup>1</sup>

### *Is There a Test for AIDS?*

The so-called AIDS test does not diagnose AIDS. An AIDS diagnosis requires actual illness, typically infections or cancers that indicate severe immune system damage. Even in the presence of such indicators (opportunistic infections like *Pneumocystis carinii* pneumonia or toxoplasmosis and cancers such as Kaposi's sarcoma or non-Hodgkins lymphoma), other possible causes of immune suppression must first be ruled out, including the use of immune suppressive or steroidal drugs or primary cancers that are themselves immune suppressive.<sup>2</sup>

Direct evidence for HIV infection would result from detecting the virus itself. Such methods, however, are used mainly for purposes of laboratory investigation.<sup>3</sup> Detection of an immune response to the virus, in the form of antibody to the virus, is the most widely used form of testing for such purposes as blood screening. But the mere presence of antibody to HIV does not establish an AIDS diagnosis, nor does it foretell with certainty the onset of HIV-related illness in the future; moreover, early detection of HIV does not lead to prevention of subsequent symptoms.<sup>4</sup>

### *Why Use Antibody Tests?*

In general, the presence of antibody is a more consistent indicator of present *or* past infection than the presence of the disease-causing pathogen itself. Antibody will remain long after the causative agent of an infection has been cleared from the body. Before much became known about the natural history of HIV infection, it seemed possible that, like many other viruses, HIV might be eliminated by some individuals' immune response. Antibody would then be the only trace of past infection or of ongoing infection with undetectably low levels of virus. It now seems that most or all individuals infected with HIV never successfully eliminate the virus altogether. But in its latent state, the virus would be undetectable by antigen tests and possibly difficult to recover by viral isolation methods. Therefore, an antibody test is the most consistent index of HIV infection available which is practical to use on a large scale for screening purposes.

### *Why Use the ELISA Technique?*

The most widely used screening method, employing an enzyme-linked immunosorbent

assay (ELISA or EIA), is relatively inexpensive (typically, less than \$5 per test for the cost of reagents and equipment), highly reproducible, and technologically adapted for processing large batches of samples with efficient, automated laboratory apparatus. In contrast, other procedures (for example, viral isolation, Western blot) have technical limitations. They usually depend on the competence, consistency, and particular recipes employed in a given laboratory<sup>5</sup> and are correspondingly more expensive. They may entail procedures that require special handling (for example, the radioactive reagents used in DNA probe studies and radioimmune precipitation). They also may be more difficult to interpret: for instance, both viral isolation and antigen tests frequently fail to detect virus in samples from truly infected individuals.<sup>6</sup>

### ***What Are Current Procedures for Testing?***

The protocol used by the Massachusetts Department of Public Health in its testing and counseling programs, and by the American Red Cross New England Region Blood Service screening program described here, is typical of testing programs across the country and internationally.<sup>7</sup>

Evaluation of a sample begins with an ELISA test. If the reactivity of the sample falls below a predetermined cutoff value standardized for the particular test kit being used, the result is judged negative, that is, no antibody detected. No further testing is undertaken. If the observed reactivity is above the cutoff value, the same sample is tested again using the ELISA procedure. When reactivity registers below the cutoff value on repeat testing — not an unusual occurrence for samples from low-risk individuals — the sample is interpreted as negative.

If the repeat ELISA test is also reactive or borderline, the sample is subjected to a more specific procedure that ordinarily has the capability to distinguish antibody to HIV from antibody to something else. The immunoblot, or Western blot, can show whether the antibody detected by ELISA binds to known classes of viral protein. The distinctive banding pattern that appears when the HIV antibody is present confirms a positive ELISA result. The lack of such a pattern indicates that antibody detected by ELISA was probably elicited by some agent other than HIV which happens spuriously to cross-react with biological material that was not eliminated when the test kit was prepared.

If the immunoblot pattern is ambiguous, for instance, if the observed bands are only very faintly perceptible, still another procedure may be employed: the immunofluorescence assay.<sup>8</sup> Cells known to be infected with HIV, along with uninfected (control) cells, are exposed to a serum sample and appropriate reagents. Infected cells will become coated with a fluorescent dye if the serum sample being tested contains HIV antibody, while uninfected control cells will show no label. Such a result is considered positive. If neither infected nor uninfected cells become labeled, the sample is considered free of HIV antibody. If both infected and uninfected cells become labeled, the meaning is ambiguous, and the outcome described as “indeterminate.”<sup>9</sup>

### ***How Accurate Are Antibody Test Results?***

We do not know definitively. ELISA test kits from commercial manufacturers score differently on tests meant to standardize their performance. In 1986, five products ranged from 98.3 to 100 percent in sensitivity, which measures a test’s ability to detect infection when it is present. They ranged from 99.2 to 99.8 percent in specificity, which indicates how well a test discriminates true infection from absence of infection.<sup>10</sup> These small percentage changes make a big difference in the proportion of false positives, as discussed

below. The most sensitive tests are the least specific.<sup>11</sup> Making comparisons is difficult, because each manufacturer's tests were standardized using different test samples, and performance varies from batch to batch, even from the same manufacturer. In a study of ELISA performance in five hundred laboratories, thirty-five of approximately seven thousand positive samples were labeled negative. The laboratories, it should be noted, were voluntarily participating in these proficiency studies, and extra care may well have been taken, since the study samples were so labeled.<sup>12</sup>

Western blot tests are even more difficult to standardize or compare, because only one commercial test has been licensed. Most laboratories that perform Western blot testing use reagents they prepare with their own procedures, and they define the standards to be used in judging whether results for a sample are categorized as positive, indeterminate, or negative.<sup>13</sup> Ten of nineteen laboratories seeking U.S. Army contracts for Western blot testing were rejected because they failed a test panel at least once.<sup>14</sup> Using panels of ambiguous samples, the College of American Physicians found 12 to 15 percent of laboratories labeling two of three reactive samples indeterminate by Western blot.

The comparative performance of immunofluorescence assays — another form of confirmatory procedure — is even less well studied than that of Western blot tests.

Although specimens used in laboratory studies to standardize the performance of HIV tests receive optimal treatment, in the real world samples may be abused.<sup>15</sup> No systematic studies have been published which examine how much mistreatment of samples is permissible before antibody testing may lead to inaccurate results, or whether error would be more likely to be in the direction of false positives or false negatives.

### *Are There Many False Positives?*

A "false positive" means that someone tests positive or shows reactivity on an antibody test even though he or she is not really infected. Even with a very low rate of false-positive test results, in a population of low-risk individuals a large proportion of those few results which are positive will falsely label as infected someone who is free of HIV.<sup>16</sup> These residual positive results are likely to remain positive on subsequent tests.<sup>17</sup> If antibody is spuriously cross-reacting with HIV, it is not likely to disappear spontaneously. Furthermore, other confirmatory tests are not likely to clarify the situation. Neither viral isolation nor antigen tests are ultimate arbiters. Failure to detect virus during viral isolation may be due to very low levels of virus, rapid death of cells harvested for culture purposes, or other sources of failure of that very exacting procedure. Failure to detect antigen may result from a latent infection in which HIV is not actively replicating, since latent virus may not be detected by antigen tests.

### *If I Test Positive, What Are the Chances I Am Truly Infected?*

The likelihood that a positive result truly indicates infection is related both to the person's level of risk and to the accuracy of the test or, customarily, combination of tests used. The lower the risk, the more likely it is that a positive result is misleading; the greater the risk, the more likely it is that a positive result is a true indicator. For instance, a female who meets blood-donor eligibility criteria and who has tested positive has only a one in seven chance of truly being infected even when the combined accuracy of ELISA and confirmatory test is as high as 99.95 percent. If the combined accuracy of the test drops to 99.50 percent, then the likelihood of true infection is 1 out of 50.<sup>18</sup> Conversely, for a sexually active gay man in Los Angeles, New York, or San Francisco, or an intravenous (IV) drug

user in Greater New York, chances are better than 99 out of 100 that a positive test result accurately indicates HIV infection.

These data make sense if we consider a simple example of two hypothetical populations — one low-risk, one high-risk — of 1,000 people each. A variety of studies suggest that roughly 1 of 1,000 members of the “general population” tested randomly in such procedures as military screening or studies of serum samples from routine hospital admissions will be found positive.<sup>19</sup> Gay men in such second-tier cities (with regard to infection rates) as Pittsburgh and Chicago have an infection rate of about 300 per 1,000. Suppose a false-positive rate of 0.1 percent, or 1 per 1,000, applied to each such group. In the first case, the chances of obtaining a true and a false-positive outcome are equal (1/1,000). Put another way, the chance that a positive test is a valid predictor of infection is 50:50.<sup>20</sup> In the second example, the likelihood of true infection when a sample tests positive is 300 times greater than the likelihood of a positive result arising from test error. In other words, in a high-risk population, the predictive value of such a test is much greater than in a low- or no-risk population.

### *How Long Does It Take for Detectable Antibody to Form After Exposure?*

The U.S. Public Health Service implies that when exposure leads to infection, three months is a sufficiently long period for antibodies to develop to detectable levels.<sup>21</sup> But it is not that simple, and the question is difficult to study. Estimates using animal models or immune responses of humans to other viruses may be invalid.<sup>22</sup>

Definitive information comes from the very few known cases of seroconversion after a needle-stick accident or a blood transfusion. But these cases, involving direct inoculation of a substantial quantity of blood, may occasion a different rate of antibody development than the more typical routes of viral exposure through sexual contact or IV drug use (in which injected blood droplets are highly diluted). Also, the speed of response may be affected if IV use itself or concomitant infections have compromised the individual’s immune system.

Published literature documents a few dozen instances of seroconversion within a few months after apparent sexual exposure in gay men.<sup>23</sup> But other examples<sup>24</sup> show latency periods prior to seroconversion among gay men of twenty-three,<sup>25</sup> thirty-four,<sup>26</sup> and thirty-six months.<sup>27</sup> Some studies of IV drug users show intervals of nine, fourteen, and eighteen months between apparent exposure and the development of detectable antibodies.<sup>28</sup> None of these studies bears on the likely interval for seroconversion in low-risk or very low dose exposures.<sup>29</sup> Also, the design and manufacture of particular test kits — for example, the amount, species, and source of HIV protein selected — may affect their sensitivity.<sup>30</sup>

Finally, viral infection and antibody response within the central nervous system — detectable by studying cerebrospinal fluid — may not be apparent from studies of serum antibody.<sup>31</sup> However, such a compartmentalization of infection and antibody response is believed to occur only rarely.

### *Are There Many False Negatives?*

We do not know. For instance, ELISA-negative sera are not routinely screened by other procedures such as the Western blot,<sup>32</sup> even though when such studies are done they reveal a rate of false negatives in the neighborhood of 1 percent or higher,<sup>33</sup> owing solely to problems in the consistency of test performance. The value of a single negative test result in establishing freedom from infection with HIV among people with a history of high-risk

behavior is questionable, since the sensitivity of the ELISA test is based on studies of low-risk individuals.<sup>34</sup>

In various situations, even the most sensitive test is ineffective, because the subject being studied, although infected, does not or cannot produce detectable antibody. It is not at all unusual, for instance, to find false-negative results in symptomatic HIV-infected patients.<sup>35</sup> In one study of “high-risk” gay men<sup>36</sup> (more likely to be infected than the general gay male population), four of the ninety-six patients studied harbored virus despite persistent negative results on antibody tests.<sup>37</sup> In another research report, two of sixty-six high-risk gay men were found to harbor virus even though their serum did not reveal antibody.<sup>38</sup> Because viral isolation procedures and antigen tests do not always identify true infection,<sup>39</sup> these results may, if anything, underestimate the rate of false negatives. In another series, 8 percent of healthy infected gay men were negative by ELISA, but their infection was detected by Western blot, which would not ordinarily be performed on ELISA-negative specimens.<sup>40</sup> This statistic is consistent with theoretical estimates of 7 percent based on current test accuracy and typical infection rates for a city like Boston.<sup>41</sup>

An example indicates why negative test results may be problematic. In one 1985 study,<sup>42</sup> a healthy twenty-four-year-old gay man was evaluated who had had 250 lifetime sexual partners but fewer than 10 since 1981. He had been receptive during anal intercourse only with 4 partners, and his last oral or anal exposure to ejaculate had occurred four years before the study. His only symptoms were swollen glands in his neck and recurrences of herpes. During the two years prior to the study, he had become consistent in the practice of “safer sex” and was clinically healthy. A series of antibody test results were negative. In view of the interval since his period of greatest risk, his adherence to protective sex guidelines, his current health, and the pattern of repeatedly negative antibody test results, even very cautious counsel would affirm that very probably he was not infected. However, upon further study, his serum was found to contain evidence of HIV even though no antibody was detectable.

### ***What About Testing Newborns and Infants?***

False-positive results are likely during the first year or so of life in an uninfected child born to an HIV-infected mother. False negatives are not unusual, at one to two years old, if the child was infected pre- or perinatally.

During the first year or more after an infant is born to an infected mother, her HIV antibody, which was transferred across the placenta, may remain detectable in the baby’s circulation.<sup>43</sup> There is, during that interval, no routine way to determine whether antibody to HIV detected in such a baby’s serum derives from passive transfer of maternal antibody or from an active response to HIV infection by the infant’s immune system. Positive results, in short, may well be misleading.

As the baby’s immune system develops and maternal antibody disappears, the child may fail to mount an antibody response to HIV if he or she has been infected since birth.<sup>44</sup> The baby’s immune system may not react to HIV that has been present during its entire life in the same way as it reacts to a foreign substance; consequently, there may be no immune response — no HIV antibody — even though the child is infected.

### ***Does Presence of Antibody Prove Infectiousness?***

Once infected, an individual probably remains infected. But an infected individual may not be producing enough virus at all times to be able to transmit it to others. Since there is

no way to know when one is highly infectious and when one is not, consistent use of risk-reduction techniques is essential for people who are HIV-positive and for anyone else who may have been exposed but who does not know his or her antibody status.

Attempts to isolate HIV from blood of antibody-positive individuals succeed about 75 percent of the time.<sup>45</sup> Because viral isolation is a difficult procedure, this statistic suggests that virus is present in any individual who shows HIV antibody reactivity, even though virus may not be recoverable from a particular specimen. On the other hand, antigen tests, which show the presence of active virus or viral fragments in the specimen being tested, may be positive in only a small fraction of individuals who display antibody reactivity.<sup>46</sup>

Another indirect source of data is epidemiological: Do individuals with positive antibody tests infect steady sexual partners when they do not follow protective sex guidelines? They do, sometimes after only a single exposure. On the other hand, about half of the steady male partners of infected men may not be infected even though the uninfected partner may have been receptive during anal intercourse with the infected partner on hundreds of occasions.<sup>47</sup> The same pattern occurs in heterosexual partners, with considerable variance from study to study.<sup>48</sup> In a recent study of heterosexual partners of people unknowingly infected by blood transfusions, 92 percent of male and 82 percent of female sexual partners — with an average, respectively, of 180 and 156 unprotected sexual contacts — escaped infection.<sup>49</sup> A pattern of steadily increasing risk to the uninfected partner is suggested by research on the female partners of hemophiliacs (70 to 90 percent of whom are believed to be infected as a result of having received contaminated blood product concentrates prior to the introduction of screening programs and heat-treatment processes). Studies of these women suggest that the likelihood of infection with HIV during unprotected sexual contact increases with the length of time the infected individual has carried the virus.<sup>50</sup> There are two possible explanations. As more contacts occur, perhaps the chances become greater that whatever combination of factors is required for transmission is present. Or, as time passes, people who carry HIV may become more infectious, perhaps because their health deteriorates to the extent that they begin to produce larger quantities of virus than their immune system can inactivate.

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## Counseling Issues

Counseling individuals seeking HIV antibody testing can accomplish two important objectives:<sup>51</sup> (1) individualized assessment of risk and delivery of tailored, specific, focused risk-reduction information; (2) assurance of fully informed consent prior to testing. Informed consent implies an assessment of whether the test can address the client's motives for testing as well as an evaluation of whether the individual feels capable of managing the test outcome, whatever it is. The question of motivation forms the starting point for the following outline of issues that ideally should be reviewed in counseling individuals seeking antibody testing.

1. Why is the individual seeking testing *now*? What triggered the decision to have the test performed?
2. How accurate is the individual's understanding of the meaning of the test in relation to his or her concerns?



3. How will test results be used? What will be the behavioral and emotional outcomes?
4. Is there a clear understanding of AIDS risk-reduction guidelines?

### *Why Seek Testing Now?*

Much can be learned by finding out not only why an individual has concluded that testing is worthwhile, but, more specifically, what immediate concern prompted the decision. Responses to that question may reveal specifically relevant circumstances in the person's life, and ways in which the person might use test results both profitably and harmfully. Some typical triggering motives include the following:

- Coercion or insistence from a partner that one be tested. (Is the partner also seeking testing? Are there issues of guilt, responsibility, power, or moral superiority underlying this pressure? Would the person seeking the test persist in seeking it without such pressure?)
- Concern about symptoms. (Has the individual consulted a physician? Can some concerns be discounted as unrelated to HIV? Will negative results cause the condition to remain untreated? Will a positive test result lead to inappropriate self-diagnosis, failure to seek medical attention, or suicide?)
- Recent notification that one has been exposed from a past partner who has tested positive or who has received a diagnosis of AIDS or AIDS-related complex (ARC). (How does this new information change anything if the individual already follows risk-reduction guidelines? If the motivation for testing is to allay anxiety that has suddenly escalated, will a negative result accomplish that? Is testing motivated by the wish that a negative result will allay guilt on the part of the infected contact?)
- Recent sexual assault, after which the individual wants to establish a "baseline" antibody status, showing that as of the time of the assault, she or he was not infected; or a past assault, as a result of which the individual wants to be sure she or he was not infected by the attacker. (Does the assault survivor understand that a baseline negative result shortly after the assault may not be definitive [since *any* other possible exposure in the months before the assault could also account for the development of a positive result in the months after the assault]? If the test is to be used in prosecuting the attacker, has a lawyer been consulted for advice about the kind of evidence and testimony that will be required to pursue such redress? Will the testing procedure itself impede the process of counseling and recovery in the weeks and months following the assault? Is the testing procedure timed in such a way that the individual will have a strong support system should the result prove positive? How will test results affect the individual's motivation to practice safer sex?)<sup>52</sup>
- Pressure from a parent or a guardian. (Does the individual's behavioral history agree with the perception of those who are applying pressure for

testing? Is the individual being tested able to distinguish his or her own best interests from the demands of those attempting to pressure him or her?)

- A specific news item or media report about AIDS. (Does the individual have an accurate understanding of the information and its context? [For instance, reports speculating about unusual or unproven modes of transmission need to be labeled as such.] Are there genuine risks that the individual has not recognized which should lead him or her to adopt risk-reduction guidelines?)

### ***Does the Individual Understand the Meaning of the Test?***

Prior to the advent of AIDS, the technical content involved in counseling — even in complex decisions regarding prenatal diagnostic procedures and outcomes — was relatively straightforward and unchanging, so that attention could be devoted to the ethical and psychological issues involved. With AIDS, the relevant technical information is not only complex and difficult, but also incomplete on many key points, and rapidly evolving. At a minimum, anyone contemplating HIV testing needs to understand the following:

- A positive test result does not mean that the individual has AIDS or necessarily will develop AIDS.
- By itself, a positive test result in an individual with medical symptoms does not explain the cause of these symptoms.
- A positive test result means that the individual should consider him- or herself able to transmit HIV to others sexually, through sharing injection equipment (for any purpose, not just the use of recreational drugs, and regardless of whether the skin is punctured intramuscularly or intravenously); during pregnancy; at delivery; and possibly through breast-feeding.
- A negative result does not necessarily *prove* that an individual is free of infection. Its meaning depends on how long a time has passed since the most recent possible incidence of exposure; even with the passage of well over a year since such an incidence, there remain some false negative results, particularly, it is assumed, among individuals at high risk.
- A positive result may not be an accurate indicator of infection in individuals with very little or no identifiable risk of exposure; there may be no ultimate standard or measure to which to appeal except monitoring one's medical status for possible HIV-related developments, while scrupulously following risk-reduction guidelines.

### ***What Will Be the Impact of Test Results?***

Not enough information is yet available about the specific personality profile or psychological determinants that characterize people who respond well or poorly to HIV testing.

Many, if not most, people who seek voluntary testing assume that they will test negative and are thus hoping for reassurance that they are not infected. Often they have not considered realistically the ways in which a positive result might affect them. Many people who

are in ongoing counseling or psychotherapy never mention their concerns about AIDS or their interest in HIV testing to their therapist. And if they do, their counselor may have encouraged them to be tested, secure in the belief that the test would reduce the client's anxiety, without ever having examined with the client the possible impact of a positive result. Certainly, the test is specifically contraindicated by a risk of suicide, homicide, or other sociopathic behavior; risk of abandoning drug treatment; or other probable adverse outcomes.

In the absence of risk of those specific adverse outcomes, it is important to try to ascertain whether the individual's behavior will be any different if he or she tests positive than if he or she tests negative. If an individual feels that he or she may be infected, risk-reduction guidelines may be appropriate whether or not she or he is tested, and whether the test is positive or negative. Using test results to make career choices or financial plans may be inappropriate, since the test is an uncertain predictor of actual illness.

If a woman or a couple is using the test to help make a decision about becoming pregnant or terminating a pregnancy, even with a positive result the best choice is not a foregone conclusion. As with any other application of the test, results must be evaluated in relation to one's history of risk. And even if a mother is truly infected, it is by no means certain that her infant will become infected; the prevailing estimate — that about 50 percent of infants born to infected mothers are also infected — averages statistics from specific studies whose estimates range from about 20 percent to as high as 80 percent. Finally, just as women may reasonably choose to bear a child knowing that it may be born with Down's syndrome, hemophilia, or Tay-Sachs disease or that it may develop Huntington's chorea, so a parent or parents may determine that the risk is acceptable of giving birth to a child that may or may not be infected and, if infected, may or may not proceed to develop AIDS.

When a principal motive for testing is reduction of anxiety, the individual must consider whether a positive outcome would greatly exacerbate his or her anxiety and whether some uncertainty actually is preferable. For an individual at very low or no risk, a positive result is unlikely and, should it occur, may be misleading because it may well be a false positive. When the risk of obtaining a false positive is about equal to the risk of actual infection (for example, for people who were transfused with one or two units of blood in a low-risk area prior to the introduction of routine blood screening in the spring of 1985), the decision about whether to proceed with testing is a difficult judgment to make.

Experience with repeat and chronic test-takers suggests that although people may expect test results to allay anxiety, for many people they do not. Sometimes people seize (appropriately or not) on the ambiguities inherent in a negative result and seek repeat testing even though no amount of testing will finally dissipate their anxiety. Some people who test negative and appear at first to be greatly relieved that they have been spared may find, with the passage of time, that they are *less* able to maintain risk-reduction behavior. They repeatedly put themselves at risk, and chronically reappear for testing as a way to "monitor" whether they have gotten infected yet.

When people seek testing as a license to abandon risk-reduction precautions, they fail to recognize that it becomes more and more likely as time goes on that each new partner will be infected. The need will become progressively greater to adopt safer sex techniques and to be sure that if drug injection equipment is used it is sterile. Although the test may allay worries about the past, for most people the greater challenge looms in the future: developing and stabilizing habits that provide continuing protection from the possibility of infection. The apparent clarity of a positive or a negative result may obscure the daunting

but necessary effort to adapt to a changing environment in which safer sex must become the norm.

### *Does the Individual Understand and Follow Risk-Reduction Guidelines?*

Few situations illustrate better than the AIDS epidemic that individuals do not fit into simple, unitary categories. Actual behaviors are more important than self-designated identity in evaluating someone's risk of exposure and, more important, in delivering risk-reduction information. A gay man who always preferred very safe sex practices may nevertheless have had an accident or illness that required multiple blood transfusions before screening was introduced. Some men with hemophilia are gay, and some gay men with hemophilia inject recreational drugs and share needles. Loving husbands and devoted fathers may sustain long-term partnerships with other men in a similar situation without defining themselves as "gay," "homosexual," or even "bisexual." Former intravenous drug users who have been clean for months or years may continue to have sexual relationships primarily with other ex-users or current users. Lesbians sometimes want a gay male friend to father a child. Some heterosexual women like anal intercourse. Heavy drinkers who black out may forget not only what kind of sex they engaged in but also the gender of their partner. It matters when and where risky behavior occurred. For instance, unprotected heterosexual intercourse with a man with hemophilia living in Pittsburgh may be much more risky than with an IV drug user in Ottawa.

Risk-reduction recipes sound simple in principle. Needle sterilization seems as easy as rinsing out a drinking glass, and lists that assort safe, possibly safe, and unsafe sex acts appear perfectly straightforward. But when people nod their heads and say, "I understand," they may be suffering under significant misconceptions, or may be finding themselves unable to talk about how hard it is to put those simple guidelines into practice.

The phrase "exchange of bodily fluids" euphemistically avoids key particulars. Saliva, sweat, and tears are far less menacing than blood or semen. "Exchange," which sounds like a bank transaction, offers little clarification about how HIV may actually infect. When the phrase "direct blood contact" is employed to clarify "exchange," it may mislead, because the important blood cells in HIV infection are white, not red. The white blood cells that HIV attacks may be present at any site of infection and inflammation, as well as locations where blood vessels are actually ruptured or penetrated.

Since the beginning of the AIDS epidemic, "promiscuity" has recurrently been cited as a key factor in HIV transmission. But an emphasis on number of partners may belie the obvious: that a mutually monogamous, unprotected sexual relationship with an infected partner is much riskier than scrupulously safe sex with a multiplicity of strangers. Gay men in monogamous relationships seem less likely to be consistent about risk-reduction guidelines than men who have nonsteady partners.<sup>53</sup> For instance, an important reason why some gay men in San Francisco continued receptive anal intercourse was that they accepted a single-minded public health emphasis on the dangers of promiscuity and "anonymous partners" and believed that having fewer sexual partners would protect them.<sup>54</sup> But statistical analysis suggests that even in 1982 the spread of HIV in that city was such that a 50 percent reduction in the number of partners per year with no change in actual sexual practices would have reduced the likelihood of exposure by only about 10 percent.<sup>55</sup>

Not all sexual contacts are consensual. Even in less coercive settings than sexual assault, the obstacles to adopting protective sexual practices may not be informational, but

situational: a woman with young children whose sole source of financial support is an abusive husband who has multiple sexual partners or a pattern of chronic needle sharing during IV drug use, or both; a family, religion, and culture that tell this woman that her fulfillment in life requires that she accede to her partner's demands; a man who obtains sexual release only after drinking so much that he cannot remember whom he has slept with or what kinds of sex he had; anyone who agrees that the measure of their love and devotion or the guarantor of monogamy in a relationship is their willingness to have unprotected sex; a sex worker (someone who is paid for sex) whose client will pay a much higher fee if he does not have to use a condom.

### ***What Are the First Reactions When People Learn Their Test Results?***

People usually react to the news of a negative result the way one would expect — with considerable relief. Surprisingly often, however, some respond with indifference, and occasionally, with almost a sense of letdown.<sup>56</sup> People who learn that their test was positive display a wider range of immediate responses, including outbursts of strong feeling, especially sorrow and anger; withdrawal; stoic acceptance; a jumble of questions and thoughts; and intellectualizing (for example, “It’s what I expected,” “Now I’ll do whatever I have to do to keep from getting sick”). It has been suggested that for some, the definitive information that one is infected may be calming because it reduces the anxiety that results from uncertainty. I have observed this response on only a few occasions. Even in the case of persons who appear most genuinely convinced that they have been infected with HIV, a positive result dashes the optimism and hope that they seem to bring with them to the test situation.

### ***Over Time, How Do People Deal with Being HIV-Antibody-Positive?***

People who have tested positive are divided about whether they ever should have had the antibody test. Those who value it feel that it has been helpful in making decisions about matters such as medical care, health maintenance, and financial planning; in setting priorities; and in helping them to affirm the relative importance of various relationships with lovers, family, and friends. They rarely, if ever, feel that testing has significantly changed their commitment to protective sex — unless one views a change from consistently safe sex to abstinence as a significant contributor to public health.

Those who regret having learned their status experience a wide range of problems.<sup>57</sup> Some persons who have tested positive describe, even years after learning their antibody status, profound — sometimes omnipresent — feelings of foreboding, gloom, and impending disaster. The resulting anxiety and depression may become self-perpetuating, particularly when such feelings are interpreted as early signs of neurological damage due to the progress of an HIV infection. In a support group I co-led for seropositive gay men, the most guarded fear, which was verbalized only in the tenth week of a twelve-week program, was the fear of literally losing one’s mind to HIV infection.

Often there is tremendous uncertainty about how to deal with a medical situation that is constantly changing. Optimistic news of an experimental treatment one day is juxtaposed the next with reports of a gloomy prognosis for anyone who is infected. It is easy to collect a portfolio of tales of insensitive, AIDS-phobic, homophobic, and drug-phobic providers in medicine, dentistry, mental health, and alternative healing modalities. But even warm, patient, trusted, sensitive providers have biases about the benefits and risks of specific

treatments, whether conventional, experimental, or alternative. This diversity of opinion may be healthy, but it imposes a burden that many medical consumers have neither the training nor the temperament to bear. Gaining sufficient knowledge to make responsible choices may become as consuming as a full-time career, and also may leave the affected person with an overwhelming and inappropriate sense of responsibility for his or her own medical fate.

People having difficulty with the knowledge that they tested positive describe struggle and pain in their relationships. Friends sometimes withdraw, perhaps out of irrational fear of exposure or anxieties triggered about their own situation. Or they may become oppressively solicitous. The issue of disclosure may become a preoccupation. Does one tell family members? Which ones, and when? Must or should one tell one's employer, and, if so, when? Gay men liken the experience to "coming out," but without the sense of joyous celebration that often accompanies acknowledging and beginning to experience one's sexual identity.

Relationships may become problematic, especially if one's current sexual partner tests negative or does not know his or her status. Does one inform any or all past sexual partners or fellow drug users? What about the possible emotional fallout: blame, guilt, sorrow, old wounds reopened? Does one tell a prospective sexual/emotional partner? Can a relative stranger be trusted with this information after only a first encounter? What about the pain of rejection if the news is shared only when the relationship has gained in closeness and significance? If the information is conveyed after a sexual encounter, even a scrupulously safe one, how does that affect trust in the future, if the relationship survives such a disclosure? If one decides to restrict sexual relations only to those who have also tested positive, how does one meet them? If one chooses celibacy, how are needs for interpersonal warmth, intimacy, and physical closeness to be met?

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## **Policies for Testing**

Testing is now one of the most popular items in AIDS budgets. Counting becomes confused with controlling.<sup>58</sup> The principal reasons for this derive as much from emotion as from reason. Everyone experiences a sense of urgency to *do something*, preferably something palpable, quick, easy, universally applicable, and mechanically predictable. The uncharitable perception endures, usually with respect to groups other than those to which authors of pro-testing recommendations belong, that "they" will change behavior only if they are somehow shocked or flogged into it by the distress of a positive test result.<sup>59</sup> The misconception persists among many policymakers that people who test negative need be less worried about transmission than those who test positive. Testing also has the effect, desirable to some, of diverting educational dollars into fiscal support of laboratories and collection of epidemiological data. A mechanical procedure like drawing blood samples and running them through a laboratory procedure seems somehow more hard-hitting, objective, and productive than education, which seems soft — just a cozy little chat about sex.

### ***Does Knowing One's Antibody Status Lead to Risk Reduction?***

Long-term reactions to learning one's antibody status remain poorly documented and mostly anecdotal. This is important, because longitudinal studies of the factors important in maintaining safer sex do not agree with cross-sectional studies.<sup>60</sup> Relatively few people

have known their HIV antibody status for more than a year or two. Many of those who have been studied are in individual therapy or support groups or research studies, all of which select subjects who are in certain ways nonrepresentative.<sup>61</sup> Some clinical interventions may select specifically for people experiencing difficulty managing this knowledge. Others may attract those who already are coping very well. Besides knowledge of antibody status, usually all subjects in such studies are receiving some form of systematic professional attention, educational interventions, and support as part of the research protocol.

What we do know is not especially encouraging. Some studies of short-term outcomes do indeed suggest that people who learn they have tested positive reduce risky behavior to a greater extent than people who have tested negative.<sup>62</sup> This is not as reassuring as it may sound — assuming that the negative result *is* a valid indicator of freedom from infection — since there remains the risk of future exposure. Other findings suggest that those who learn they have tested negative may be less committed to adopting safer behavior than those who do not learn their antibody status.<sup>63</sup> Although the U.S. Public Health Service suggests that learning one's antibody status is “an important component of prevention strategy” for individuals with a history of high-risk behavior, presumably because it will motivate them to make a concerted effort to reduce risk,<sup>64</sup> the most methodologically sound research studies to date suggest that, at least for gay men, other factors besides knowledge of one's antibody status weigh more heavily in the consistent, sustained practice of safer sex.<sup>65</sup> Of great importance to these persons is the perception that they are situated in a supportive peer community that holds shared values about the importance of safer sex. Paradoxically, persons with the greatest sense of vulnerability to AIDS — such as those who have tested positive — may have the greatest difficulty in adjusting to and maintaining safer practices.<sup>66</sup> Individuals already having difficulty with impulse control — who have not integrated knowledge of risk reduction with behavior — may not become more cautious upon learning they are infected with HIV.<sup>67</sup> This is consistent with the observation that intravenous drug users who are in the early weeks of drug treatment and who learn they are antibody-positive are more likely to drop out of such programs or return to injecting drugs, or both, than if they learn they are antibody-negative or do not learn their antibody status.<sup>68</sup> Anecdotally, people who have been in recovery from drug addiction for a year or more have remarked to me that they doubt they could have handled news of a positive antibody status during their first three to six drug-free months.

### ***Should All Members of “High-Risk” Groups Be Tested?***

Antibody screening has been recommended for *all* members of so-called high-risk groups and is required of any captive or disenfranchised populations available to the federal and various state governments, including immigrants seeking to become naturalized citizens; prisoners; and military, Peace Corps, Vista, and all foreign service personnel. In a pioneering analysis of HIV antibody screening programs,<sup>69</sup> Bayer et al. have stipulated ethical principles and have located pragmatic grounds for rejecting mass screening for hospital admissions (except perhaps in custodial institutions), marriage, prison, or the workplace (except perhaps “prostitutes”).<sup>70</sup> Most public health officials concur, sharing concerns about the accuracy and efficacy of tests, the relative costs in comparison with other prevention interventions, and legal as well as ethical implications.<sup>71</sup>

But, setting aside three basic principles that they propose — “respect for persons,” “beneficence,” and “justice” — Bayer et al. focus on a fourth, “the harm principle,” and deny that individuals at high risk should have “the right not to know” their antibody sta-

tus. They argue for use of the antibody test because “there is reason to doubt that advice alone provides sufficient motivation” for “radical alterations in sexual conduct and in childbearing plans. . . . Given the risks associated with AIDS and the uncertainty about what will in fact modify high-risk behavior, there is a strong community interest in encouraging voluntary testing.” The authors acknowledge, however, that “such information may be so psychologically devastating that the individual will suffer greatly without any benefits to himself or herself or additional benefits to others.”<sup>72</sup>

I believe their position is flawed for three reasons. First, the argument poses a false dichotomy: we are not forced to choose between advice and testing. Another option must be made available for anyone — aware of their antibody status or not — having difficulty reducing high-risk behavior or in danger of relapse: sensitive, responsive, creative programs that support the process of achieving a satisfying adaptation to the requirements for sexual risk reduction.<sup>73</sup> Second, why assume that when “advice” does not effect behavioral change, “information” — in the form of knowledge of one’s antibody status — will? This is particularly problematic, for reasons given by Bayer et al.: “There is no way to discern in advance which of the infected people will modify their behavior without notification and which will not,”<sup>74</sup> nor, I would add, is there a way to discern in advance which persons, given notification, will modify their behavior in harmful ways.

Third, Bayer et al. institute a revealing double standard. For health care providers performing invasive procedures, a risk of HIV transmission exists which is more than “only theoretical,” for instance, if an accident exposes the open wound of a patient to blood from a health care worker. Health care personnel are advised to take “standard infection control precautions . . . whether or not they know their antibody status.”<sup>75</sup> Such precautions are futile for accidents in which blood is drawn — for example, when a blade slips and cuts through single or double latex gloves. Why not here, too, accord priority to the harm principle and argue forcibly for submission to voluntary testing by all health personnel who perform invasive procedures? Why suppose that knowledge of one’s antibody status is an indispensable motivator for sexual risk reduction but has no bearing on scrupulousness about infection control, no influence on the care taken to avoid accidents, and no relevance to the desirability of voluntary job reassignment for HIV-infected health personnel performing invasive procedures? The point here is not to argue that health care workers performing invasive procedures have no right to remain uninformed of their antibody status, but rather to suggest that there is serious inequity in denying “the right not to know” to conventionally defined high-risk groups while implicitly extending it to everyone else.<sup>76</sup>

### *How Should Testing Programs Be Evaluated?*

To the ethical principles Bayer et al. propose in their analysis of screening programs, I suggest adding two criteria for the evaluation of testing proposals: (1) that they are the least intrusive way to accomplish a necessary goal, and (2) that they obey the fundamental dictum of medicine to do no harm.

As an example of the first principle, the need for epidemiological data on rates of infection can be met without testing and labeling specific individuals as infected. Blind samples, coded by source (for example, inner-city vs. rural newborn infant blood samples used in an ingenious study of childbearing women in Massachusetts<sup>77</sup>) can reveal a great deal about infection rates in the general population, and voluntary testing programs as well as noncoerced participation in research studies already have provided much information, not only about overall rates of infection, but about the dynamics of HIV transmission.



The second principle encapsulates the problem with widespread use of HIV testing as a means of effecting behavior change: it is a psychologically invasive procedure of unproven benefit. Although no physically invasive procedure — chemotherapy, surgery, or other medical treatment — is widely adopted without evaluating whether its anticipated benefit equals or exceeds its risk, HIV testing has not been so stringently reviewed. Yet it is sufficiently psychologically intrusive to have been the immediate precipitating factor for some suicides. And it is experimental — of uncertain benefit and of unknown risk in terms of long-term adverse psychological sequelae.

The cautious evaluation of drugs used to treat patients with AIDS models appropriate care in evaluating unproven treatments. The medical profession weighs seriously the physical harm done by a drug with dangerous side effects, even though human compassion and the danger of imminent death both dictate the most expansive availability of any promising therapeutic agent for AIDS. In contrast, advocates of testing programs may cavalierly dismiss psychological morbidity.<sup>78</sup> They may never even mention that an evaluation plan needs to be implemented for analyzing outcomes, and weighing their risks and benefits.<sup>79</sup>

Drug trials offer a valid paradigm for considering risky, unproven psychological interventions. Although Suramin was an effective antiviral agent in the test tube, it apparently did more harm than good when employed on a small sample of people with AIDS: careful, skeptical evaluation was essential to spare people from misuse of a drug that appeared at first to be promising. When Azidothymidine (AZT, or zidovudine, or Retrovir) was shown in the laboratory to be of apparent benefit in inhibiting the growth of HIV, it was distributed widely to AIDS patients only after two phases of trials: one to identify whether a dose existed that the human body could tolerate without irreversible harm, and a second to establish whether treatment conferred any benefit. In that second phase, parallel double-blind placebo-controlled studies enrolled patients from specific subgroups.<sup>80</sup> On the basis of such studies, AZT currently is recommended only for persons with AIDS as diagnosed by a history of *Pneumocystis carinii* pneumonia and for persons with helper T-cell counts below a specified threshold. Without sufficient evidence of benefit for other subgroups, AZT is not routinely recommended for all people with AIDS, much less all people infected with HIV.

Compare that caution and specificity with the blanket recommendation that all individuals in so-called high-risk groups seek voluntary HIV antibody testing, or with arguments for even more widespread mandatory testing (sometimes euphemistically referred to as “required” testing). We need to know how intravenous drug users react who are not in treatment, who are in methadone programs, who are now drug-free, who are in Alcoholics Anonymous, Narcotics Anonymous, or other twelve-step recovery or self-help programs, who are breadwinners for families, who are in shelters for the homeless or in community housing, who are living alone, and so on. We need to know how gay men in long-term monogamous relationships react to test results, compared to gay men who are not, compared to married bisexual men. We need to know how test results affect gay men still practicing high-risk sex with various partners, compared with gay men who are practicing high-risk sex only with long-term monogamous partners, compared with gay men who routinely are essentially safe in sexual behavior. Hardly any information exists about the specific psychological profile — in terms of such factors as locus of control, risk taking, capacity for intimacy, tolerance for ambiguity, self-esteem, and so on — of persons likely to benefit from testing. And until such research is done, it is no more ethical to

prescribe antibody testing for all members of high-risk groups than it would have been to recommend AZT for everyone infected with HIV.

Public health policies that endorse widespread or “routine” testing may compound the problems already experienced by health educators who deal with AIDS. A single example may suffice. Mistrust of medical expertise already accounts for unyielding public concern about AIDS transmission via casual contact. What will be the effect on public trust and public policy of testing programs that falsely label half of those who test positive as infected carriers of a lethal virus, while erroneously reassuring thousands of infected people who test negative that they have nothing to worry about? 🐼

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## Notes

1. The views expressed in this article do not necessarily represent those of the Massachusetts Department of Public Health.
2. Only in the most recent modification of the Centers for Disease Control surveillance definition of AIDS has the “AIDS test” in certain circumstances become a necessary part of the differential diagnosis of AIDS. It is employed where an individual with a history suggesting possible exposure to HIV is severely ill — for instance, having lost 10 percent of body weight, with chronic diarrhea or fatigue, or dementing — and no other specific explanation can be found other than infection with HIV. “Revision of the CDC Surveillance Case Definition for Acquired Immunodeficiency Syndrome,” *Morbidity and Mortality Weekly Report* (supplement) 36, no. 1S, 14 August 1987.
3. Limitations of each of the principal methods for establishing the presence of the virus restrict their usefulness for screening purposes.
  - a. Microscopy: If HIV is not actively reproducing and is instead in a latent state, it will not appear under microscopic observation. Even if it is actively replicating, it still may be present in such a small proportion of cells that it will escape observation.
  - b. Viral isolation: The growth of HIV from a tissue specimen or body fluid sample does prove that the virus is present. But growing sufficient virus to be detected takes time, requires skill, and often does not yield reproducible results. Thus, viral isolation may underestimate the presence of virus in a truly infected specimen.
  - c. Antigen testing: If HIV is latent — incorporated in its “proviral” form into the DNA of an infected cell — there will be no reactivity on an antigen test. Because antigen tests most accurately measure active HIV infection, a principal use of antigen testing is to evaluate the effect of antiviral agents on viral replication.
  - d. DNA probe (Southern blot; *in situ* hybridization): Fragments of viral DNA in the chromosome can be detected by the binding of radioactively labeled or colorimetrically detectable probes constructed of complementary DNA sequences. The proportion of chromosomal DNA in an infected cell contributed by viral genes is very small, as is the proportion of cells actually infected with HIV. Some method of amplifying the amount of viral DNA is necessary so that it can be detected. Such a method has only recently been developed for laboratory use. See Jeffrey L. Fox, “Monitoring and Diagnosis of HIV,” *American Society for Microbiology News* 53 (1987): 430. The technical difficulty of handling radioactive materials makes this procedure costly and not now widely applicable.
  - e. Indicator cell lines: This procedure depends on the conservation of special regulatory genes and proteins among variant strains of HIV which are not found in other viruses. It is more complicated than current antigen or antibody tests but would detect latent as well as active infection. See Barbara K. Felber and George N. Pavlakis, “A Quantitative Bioassay for HIV-1 Based on Trans-Activation,” *Science* 239 (1988): 184–186.

4. Kenneth H. Mayer, "The Clinical Challenges of AIDS and HIV Infection," *Law, Medicine and Health Care* 14 (1986): 281–289.
5. Commercial Western blot reagents manufactured by DuPont have been licensed during the past year but cost more than laboratories spend preparing the equivalent materials using their own procedures. Consequently, cost savings override the possible benefits of standardization, in practice.
6. Kenneth H. Mayer et al., "Correlation of Enzyme-Linked Immunosorbent Assays for Serum Human Immunodeficiency Virus Antigen and Antibodies to Recombinant Viral Proteins with Subsequent Clinical Outcomes in a Cohort of Asymptomatic Homosexual Men," *American Journal of Medicine* 83 (1987): 208–212.
7. "Update: Serologic Testing for Antibody to Human Immunodeficiency Virus," *Morbidity and Mortality Weekly Report* 36, no. 3 (8 January 1988): 833–845.
8. F. K. Mundon et al., "Analysis of Discrepant Anti-HIV ELISA Reactives," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract TP. 248, p. 103.
9. In such ambiguous situations, which have occurred in less than 1 percent of samples evaluated thus far in voluntary screening programs in Massachusetts, another sample is usually requested. If the ambiguity resulted from very low levels of antibody developing in the early stages of infection, a sample drawn four to eight weeks later should be plainly reactive. If the ambiguity resulted from low levels of cross-reactive antibody first elicited by something other than HIV, the borderline or ambiguous results would persist after such a time delay (workshop presentation by Victor Berardi, Director of Virology, Massachusetts Department of Public Health, State Laboratory Institute, Jamaica Plain, Massachusetts, 4 January 1988).
10. Paul D. Cleary et al., "Compulsory Premarital Screening for the Human Immunodeficiency Virus: Technical and Public Health Considerations," *Journal of the American Medical Association* 258 (1987): 1757.
11. *Ibid.*
12. "Update: Serologic Testing" (note 7).
13. Klemens B. Meyer and Stephen G. Pauker, "Screening for HIV: Can We Afford the False Positive Rate?" *New England Journal of Medicine* 317 (1987): 238–241; also, "Update: Serologic Testing" (note 7).
14. Roger N. Taylor et al., "Summary of the Centers for Disease Control Human Immunodeficiency Virus (HIV) Performance Evaluation Surveys for 1985 and 1986," *American Journal of Clinical Pathology* 89 (1988): 1–13. See also Cleary et al. (note 10).
15. Long periods of time may pass before the serum used in ELISA testing is separated by centrifugation from blood cells. If the cells break down before serum is separated, some breakdown products (hemolysis) may affect the structural integrity of serum antibody. Bacterial contamination of samples, particularly if they are left unrefrigerated for several days (as may occur if samples are sent by surface mail), may also affect serum antibody.
16. Meyer and Pauker (note 13).
17. False-positive results can occur for a variety of reasons. Every individual has the potential to produce antibodies of millions of different specificities; from a lifetime of exposures to foreign antigens, we may each carry antibody of thousands of different specificities. Some people even make antibody to polystyrene, the plastic substrate used in several commercial ELISA test kits! (Confirmatory Western blotting would rule out that source of reactivity as HIV-related, however.) Antibody elicited by one sort of foreign entity and strongly reactive to it may happen to react, to a lesser degree, with other molecules as well: antibodies do not, after all, "know" with what they should and should not react. In screening thousands of individuals, it is therefore not surprising to turn up dozens who have antibody that happens to react to some portion of HIV or to materials used in test kits and who thus appear to test positive even though they have never been exposed to the virus. Such false-positive results are even likelier among those who (1) have been exposed

to unusually large amounts of diverse antigens or (2) have a disease process that results in unusually large quantities of antibody. An explanation of each category follows.

Drug injections with equipment that has not been sterilized may include such foreign materials as blood cells and plasma proteins from others. Proteins and other components of semen emitted during anal intercourse may enter the bloodstream through ruptured capillaries in the anorectal canal. Ordinary blood transfusions and the concentrated blood products used in the treatment of hemophilia contain massive quantities of foreign antigen. Although these potential sources of false-positive results bear more heavily on members of the main risk groups, the higher prevalence of infection in such groups makes it likely nevertheless that a positive test result accurately indicates HIV infection. To its pregnant mother a fetus is, immunologically, a large transplant of foreign tissue. Ordinarily, the placenta keeps the mother from rejecting the fetus but, especially at delivery, the mother's circulation may be exposed to fetal cells. This mechanism explains why women who have had many pregnancies may be somewhat likelier to test positive for HIV antibody although they have never been exposed to the virus. See Jay B. Hunter and Jay E. Menitove, "HLA Antibodies Detected by ELISA HTLV-III Antibody Kits" (letter), *Lancet* 2 (1985): 397.

Abnormally large amounts of antibody produced by patients with systemic lupus erythematosus and rheumatoid arthritis may cross-react with the antigens used in HIV tests. Injections of immune globulin may cause transient reactivity. See Paul D. Cleary et al., "Compulsory Premarital Screening for the Human Immunodeficiency Virus: Technical and Public Health Considerations," *Journal of the American Medical Association* 258 (1987): 1757. Although no such false-positive results were observed in the few samples from such patients during initial evaluations of ELISA test specificity, in studies of larger numbers of patients with no known risk of HIV exposure, some samples have been found to be reactive. Failure to clear antibody from the circulation — for instance, as a result of liver damage caused by very high levels of alcohol consumption or chronic active hepatitis — may also lead to unusually high levels of antibody. See C. J. Mendenhall et al., "False Positive Tests for HTLV-III Antibodies in Alcoholic Patients with Hepatitis," *New England Journal of Medicine* 314 (1986): 921–922, and F. R. Cockerill et al., "'False Positive' Antibodies to Human Immunodeficiency Virus (HIV) Detected by an Enzyme-Linked Immunosorbent Assay (ELISA) in Patients at Low Risk for Acquired Immune Deficiency Syndrome (AIDS)," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract MP.147, p. 34. Moreover, since all biological materials spontaneously degrade, those antibodies which remain longest in the circulation may have altered specificity — they may become more "sticky" — which would cause them to react with HIV test antigens. Other mechanisms are mentioned in connection with an elevated association between anti-HIV and antimalarial antibody in African subjects. See Robert J. Biggar et al., "ELISA HTLV Retrovirus Antibody Reactivity Associated with Malaria and Immune Complexes in Healthy Africans," *Lancet* 2 (1985): 520–523.

18. Meyer and Pauker (note 13).

19. Jeffrey L. Fox, "AIDS: the Public Health–Public Policy Crisis," *American Society for Microbiology News* 53 (1987): 426–430; Department of Health and Human Services, U.S. Public Health Service, "Human Immunodeficiency Virus Infections in the United States: A Review of Current Knowledge and Plans for Expansion of HIV Surveillance Activities. A Report to the Domestic Policy Council," November 30, 1987; "Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus Antibody Prevalence in U.S. Military Recruit Applicants," *Morbidity and Mortality Weekly Report* 35: 421–428; and Rand L. Stoneburner et al., "Risk Factors in Military Recruits Positive for HIV Antibody" (letter), *New England Journal of Medicine* 315 (1986): 1355.

20. Cleary et al. (note 10) believe that the proportion of false-positive results may be as high as 85 percent under certain real-world testing situations.

21. "Public Health Service Guidelines for Counseling and Antibody Testing to Prevent HIV Infection and AIDS," *Morbidity and Mortality Weekly Report* 36: 510–515.

22. Humans may respond differently to HIV than primates (which do not appear to get AIDS after infection with HIV). See R. Yanagihara et al., "Attempts to Produce a Progressive Immune Deficiency and Encephalopathy in Nonhuman Primates with the Human Immunodeficiency Viruses," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Ab-

- tract TP.29, p. 67. The time required for an immune response to other viruses such as hepatitis B may be misleading, because most inocula of HBV contain larger quantities of virus than inocula of HIV. Also, HBV is not a retrovirus; HIV is. That means HBV does not, like HIV, enter a latent phase during which it is inactive, incorporated into the DNA of its host's immune cells, and not immunogenic. Because infection with HBV means that large amounts of virus are available to stimulate an immune response, the time course of response to infection with HBV is likelier to be more predictable and more rapid than with HIV.
23. For instance, see Hans Gaines et al., "Antibody Response in Primary Human Immunodeficiency Virus Infection," *Lancet* 1 (1987): 1249–1253, whose subjects required two to seven weeks to seroconvert.
  24. Jean-Pierre Allain et al., "Serologic Markers in Early Stages of Human Immunodeficiency Virus Infection in Haemophiliacs," *Lancet* 2 (1986): 1233–1236, observe a series of six seroconversions requiring 1, 1, 3.5, 3.5, 5, and 9 months, respectively.
  25. C. M. Farber et al., "Persistent Human Immunodeficiency Virus (HIV) Detection in Seronegative Asymptomatic Carriers," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract MP.124, p. 30.
  26. Annamari Ranki et al., "Long Latency Precedes Overt Seroconversion in Sexually Transmitted Human Immunodeficiency Virus Infection," *Lancet* 2 (1987): 589–593. Persistent HIV antigen or very low levels of core antibody were detected in seven of forty-seven gay men and in one woman who tested nonreactive on conventional ELISA tests. Three of the seven showed a defect in cell-mediated immunity, which may account for their delayed or indolent antibody response. (Both underlying cancer and immunosuppressive drugs may cause a loss of antibody reactivity on ELISA tests. See Richard G. Marlink et al., "Low Sensitivity with ELISA Testing in Early HIV Infection" (letter), *New England Journal of Medicine* 315 (1986): 1549–1550. However, false-negative results remain a concern for individuals at high risk, whether or not a state of immunocompromise lengthens the time required to seroconvert.
  27. Harold A. Kessler et al., "Diagnosis of Human Immunodeficiency Virus Infection in Seronegative Homosexuals Presenting with an Acute Viral Syndrome," *Journal of the American Medical Association* 258 (1987): 1196–1199. The case report reads as follows: "Patient 3 had been in a strictly monogamous relationship for three years and practiced 'safe sex' with his partner, who was asymptomatic and negative for HIV by culture and serologic analysis for antibody and antigen. This suggests that this patient, who was also HIV culture positive, may have been asymptotically infected for up to three years before the onset of his acute syndrome."
  28. The form of antibody produced during a primary or initial immune response to HIV (IgM) is not detected by conventional antibody tests. Normally, this is not a problem, because IgM antibody typically disappears in several weeks, and is replaced by a more stable form of serum antibody (IgG) that is detected by conventional antibody tests. However, sometimes the primary-response IgM antibody species remains for many months and is not detected by conventional antibody tests for IgG even though the individual is infected during the entire period. G. Bedarida et al., "HIV IgM Antibodies in Risk Groups Who Are Seronegative on ELISA Testing," *Lancet* 2 (1986): 570–571, and "Anti-IgM Screening for HIV," *ibid.*, p. 1456. One infected, HIV-IgM-positive subject in this series still had not developed detectable IgG antibody at 18.5 months of follow-up.
  29. Kenneth H. Mayer, "The Epidemiological Investigation of AIDS," *Hastings Center Report*, August 1985, pp. 12–15. A detailed sexual and drug history and serial tests for antibody, alongside multiple tests for virus or antigen, would yield more reliable norms concerning the rate of false-negative antibody results by risk group and the time intervals between exposure, infection, and seroconversion. This has been done only in one study (see note 26), and it would require hundreds or possibly thousands of subjects as well as great expense for the battery of laboratory tests necessary to cross-verify whether subjects actually harbor HIV.
  30. A test that performs with excellent sensitivity in low-risk populations may be less reliable in assaying high-risk samples. See L. Grillner et al., "False-Negative Result by the Wellcozyme Anti-HIV Assay in Testing an HIV-Positive Haemophiliac," *Lancet* 1 (1987): 1200–1201.

31. Mark S. Greenberg, "Neuropsychological Manifestations of AIDS" (lecture, Harvard University), 17 December 1987.
32. National Institutes of Health, "The Impact of Routine HTLV-III Antibody Testing on Public Health," Consensus Development Conference Statement 6, no. 5, *Journal of the American Medical Association* 256 (1986): 1778–1783.
33. Dana Gallo et al., "Comparison of Detection of Antibody to the Acquired Immune Deficiency Syndrome Virus by Enzyme Immunoassay, Immunofluorescence, and Western Blot Methods," *Journal of Clinical Microbiology* 23 (1986): 1049–1051.
34. Michael J. Barry, Paul D. Cleary, and Harvey V. Fineberg, "Screening for HIV Infection: Risks, Benefits, and the Burden of Proof," *Law, Medicine and Health Care* 14 (1986): 259–268.
35. Jerome E. Groopman, "Clinical Spectrum of HTLV-III in Humans," *Cancer Research* 45, Suppl. 9 (1985): 4649s–4651s; and James R. Carlson et al., "AIDS Serology Testing in Low- and High-Risk Groups," *Journal of the American Medical Association* 253 (1985): 3405–3408.
36. These "high-risk" gay men were selected because they were believed to be most likely to be infected although antibody-negative: they had been sexual partners of infected individuals, or had had hundreds of sexual partners, or showed laboratory signs of immune system aberration while being clinically healthy.
37. S. Zaki Salahuddin et al., "HTLV-III in Symptom-Free Seronegative Persons" (letter), *Lancet* 2 (1984): 1418–1419.
38. Kenneth H. Mayer et al., "Natural History of HTLV-III/LAV Infection in Asymptomatic Male Homosexuals in Boston" (abstract), International Conference on Acquired Immune Deficiency Syndrome, Paris, 23–25 June 1986.
39. The same research laboratory was able to detect HIV in only 43 percent of seropositive subjects. See D. D. Ho et al., "Primary Human T-Lymphotropic Virus Type III (HTLV-III) Infection," *New England Journal of Medicine* 313 (1985): 1606.
40. Groopman (note 35), p. 3405.
41. Barry et al. (note 34).
42. Kenneth H. Mayer et al., "Human T-Lymphotropic Virus Type III in High-Risk, Antibody-Negative Homosexual Men," *Annals of Internal Medicine* 104 (1986): 194–196.
43. J. Q. Mok et al., "Infants Born to Mothers Seropositive for Human Immunodeficiency Virus," *Lancet* 1 (1987): 1164–1168.
44. W. Borkowsky et al., "Human Immunodeficiency Virus Infections in Infants Negative for Anti-HIV by Enzyme-Linked Immunoassay," *Lancet* 1 (1987): 1168–1171; Kwang Ho Pyun et al., "Perinatal Infection with Human Immunodeficiency Virus," *New England Journal of Medicine* 317 (1987): 611–614; and Leonard R. Krolov et al., "Longitudinal Serologic Evaluation of an Infant with Acquired Immunodeficiency Syndrome," *Pediatric Infectious Disease Journal* 6 (1987): 1066–1067.
45. In the earliest attempts to isolate HIV (then called HTLV-III or LAV or ARV), the virus was detected in 30 to 54 percent of adult AIDS patients and in 50 to 86 percent of "pre-AIDS" (ARC) patients. Robert C. Gallo et al., "Frequent Detection and Isolation of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and at Risk for AIDS," *Science* 224 (1984): 500–502; and Jay A. Levy et al., "Isolation of Lymphocytopathic Retroviruses from San Francisco Patients with AIDS," *Science* 225 (1984): 840–842.
46. J. A. M. Lange et al., "Viral Gene Expression, Antibody Production and Immune Complex Formation in Human Immunodeficiency Virus Infection," *AIDS* 1 (1987): 15–20; and Deborah A. Paul et al., "Correlation of Serum HIV Antigen and Antibody with Clinical Status in HIV-Infected Patients," *Journal of Medical Virology* 22 (1987): 357–363.
47. Kenneth H. Mayer, "Male Homosexual Transmission of HIV Infection," Annual Meeting of the American Association for the Advancement of Science (Boston), 11–15 February 1988.

48. Gerald H. Friedland and Robert S. Klein, "Transmission of the Human Immunodeficiency Virus," *New England Journal of Medicine* 317 (1987): 1125–1135.
49. Thomas A. Peterman et al., "Risk of Human Immunodeficiency Virus Transmission from Heterosexual Adults with Transfusion-Associated Infections," *Journal of the American Medical Association* 259 (1988): 55–58.
50. James Goedert, "Natural History of HIV Infection," Annual Meeting of the American Association for the Advancement of Science (Boston), 11–15 February 1988.
51. See also for general guidelines and suggestions Gabriele Dlugosch, Marc Gold, and James Dilley, "AIDS Antibody Testing: Evaluation and Counseling" and "Diagnosis/Treatment: Disclosing AIDS Antibody Test Results," *Focus* 1, no. 8 (July 1986): 1–3; Peter Goldblum and Neil Seymour, "Whether to Take the Test: Counseling Guidelines," *Focus* 2, no. 5 (April 1987): 1–3; Stephan L. Buckingham, "The HIV Antibody Test: Psychosocial Issues," *Social Casework* (September 1987): 387–393; and Mark Gold, Neil Seymour, and Jeffrey Sahl, "Counseling HIV Seropositives," in *What to Do About AIDS*, ed. Leon McKusick (Berkeley: University of California Press, 1986), pp. 103–110.
52. These issues, which have not been much discussed in print, grew out of planning discussions and plenary and workshop sessions of a recent conference entitled AIDS and Rape (Needham, Massachusetts), 7 January 1988.
53. Leon McKusick et al., "Prevention of HIV Infection Among Gay and Bisexual Men: Two Longitudinal Studies," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, p. 213.
54. David G. Ostrow et al., "Sexual Behavior Change and Persistence in Homosexual Men," *International Conference on Acquired Immunodeficiency Syndrome* (Atlanta, Georgia), 14–17 April 1985 (Session 26.3), p. 71.
55. J. M. Van Druuten et al., "AIDS Prevention and Intervention," *Lancet* 1 (1986): 852–853.
56. This observation is based on the author's experience with delivering antibody test results to over 1500 individuals in the greater Boston area. See also Susan D. Cochran, who concluded, from a study of 150 asymptomatic gay men, that "knowledge of a positive HTLV-III/LAV result may have negative consequences for psychosocial functioning, but a negative result does not lead to less distress than not knowing," in "Psychosomatic Distress and Depressive Symptoms Among HTLV III/LAV Seropositive, Seronegative, and Untested Homosexual Men," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract MP. 202, p. 43.
57. Cochran (note 56) and Dlugosch et al. (note 51).
58. This is pointed out in Barry et al. (note 34).
59. An unfortunate example was recently published by a member of the President's Commission on the HIV Epidemic: Theresa L. Crenshaw, "HIV Testing: Voluntary, Mandatory, or Routine?" *Humanist* (January–February 1988): 29–34.
60. Jill G. Joseph et al., "Magnitude and Determinants of Behavioral Risk Reduction: Longitudinal Analysis of a Cohort at Risk for AIDS," *Psychology and Health* (in press).
61. Laura Dean and J. L. Martin, "Differential Participation Rates and Epidemiologic Estimates of AIDS," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract THP. 79, p. 176. The authors conclude that "the highest risk individuals, the highest rates of HIV infection, and the highest rates of AIDS are to be found in the subset of individuals who never enroll or are unwilling to continue participation in behavioral and serologic AIDS studies." By extension, those most harmed by testing procedures may be least accessible to follow-up.
62. See Dlugosch et al. (note 51) and Thomas J. Coates, S. F. Morin, and Leon McKusick, "Consequences of AIDS Antibody Testing Among Homosexual Men: The AIDS Behavioral Research Project," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract WP. 184, p. 141.

63. Robin Fox, N. Odaka, and B. F. Polk, "Effect of Learning HTLV-III/LAV Antibody Status on Subsequent Sexual Activity," *III International Conference on AIDS Abstracts Volume* (Paris), 23–25 June 1986, Session S18d, p. 167. "Disclosure of a negative Ab test," in comparison with testing positive or not learning one's status, "did not result in a comparable reduction in sexual activity. . . . [T]he effect of informing gay men of their Ab status may be contrary to the goal of public health programs, which is to decrease the spread of HTLV-III/LAV through sexual activity."
64. "Public Health Service Guidelines" (note 21). See also Thomas J. Coates, Stephen F. Morin, and Leon McKusick, "Behavioral Consequences of AIDS Antibody Testing Among Gay Men" (letter), *Journal of the American Medical Association* 258 (1987): 1889.
65. Joseph (note 60); Karolynn Siegel et al., "Factors Distinguishing Homosexual Males Practicing Safe and Risky Sex," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract TP. 171, p. 91; and (in Vancouver, BC, Canada) Brian Willoughby et al., "Sexual Practices and Condom Use in a Cohort of Homosexual Men: Evidence of Differential Modification Between Seropositive and Seronegative Men," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Session M.6.3, p. 5.
66. Jill G. Joseph et al., "Perceived Risk of AIDS: Assessing the Behavioral and Psychosocial Consequences in a Cohort of Gay Men," *Journal of Applied Social Psychology* (submitted), and Carol-Ann Emmons et al., "Psychosocial Predictors of Reported Behavior Change in Homosexual Men at Risk for AIDS," *Health Education Quarterly* 13 (1986): 331–345.
67. Marshall Forstein, director of outpatient psychiatry, Cambridge Hospital, and medical director, Gay and Lesbian Counseling Service, Boston, "Why HTLV-III Antibody Testing May NOT Be Best for Everyone," 1986 (Xerox), 4 pp.
68. Richard G. Marlink et al., "High Rate of HTLV-III/HIV Exposure in IVDA's from a Small-Sized City and the Failure of Specialized Methadone Maintenance to Prevent Further Drug Use," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Session TH.5.1, p. 156.
69. Ronald Bayer et al., "HIV Antibody Screening: An Ethical Framework for Evaluating Proposed Programs," *New England Journal of Public Policy* 4, no. 1 (Winter–Spring 1988): 173–187. This article, in its original version, appeared in the *Journal of the American Medical Association* 256, no. 13 (October 3, 1986): 1768–1774, and permission to reprint the article was granted by the *Journal of the American Medical Association*.
70. *Ibid.*
71. Cleary et al. (note 10); Barry et al. (note 34); and Nan D. Hunter, "AIDS Prevention and Civil Liberties: The False Promise of Proposals for Mandatory Testing," American Civil Liberties Foundation, June 1986 (Xerox), 23 pp.
72. Bayer et al. (note 69).
73. Coates, Morin, and McKusick (note 64). Information alone is not enough: see, for instance, Jeffrey A. Kelly et al., "Relationships Between Knowledge about AIDS and Actual Risk Behavior in a Sample of Homosexual Men: Some Implications for Prevention," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract MP.174, p. 39. Nor is knowledge of antibody status enough to consistently motivate safer behavior: for instance (in addition to sources in note 66), see Jane McCusker et al., "Changes Over Time in Anogenital Practices in a Cohort of Homosexual/Bisexual Men," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1–5 June 1987, Abstract WP.172, p. 139. See, for commentary, Paul R. Gustafson, "Prevention of HTLV-III Infection" (letter), *Journal of the American Medical Association* 256 (1986): 346–347.
74. Bayer et al. (note 69).
75. *Ibid.*



76. This inequity is underscored by the issue of consent. Men having sex together, for instance, have been well warned of the risk of sexual exposure. Arguably, the entire population has been warned about risks of unprotected sex and failure to use sterile drug-injection equipment. In contrast, patients are not warned that on the average, 6 percent of health care workers are infected and the rate of infection among health care workers not attributable to conventional risks (for example, sexual, needle exposure) is almost twice that for the rest of the population (5 percent vs. 3 percent [data presented by Brian Saltzman, "HIV Transmission by Casual Contact and among Health Care Workers," Annual Meeting of the American Association for the Advancement of Science (Boston), 12-15 February 1988]). That is, two to three health care workers per thousand carry HIV and have no reason to suspect that they do so.
77. Charles Marwick, "HIV Antibody Prevalence Data Derived from Study of Massachusetts Infants," *Journal of the American Medical Association* 258 (1987): 171-172.
78. Crenshaw (note 59).
79. Cochran (note 56); Roger Stempel et al., "Patterns of Distress Following HIV Antibody Test Notification," *III International Conference on AIDS Abstracts Volume* (Washington, D.C.), 1-5 June 1987, Abstract WP.199, p. 143; and Calvin Pierce, "Several Suicides Follow Positive Tests, Under-score Urgency of HIV Counseling," *Clinical Psychiatry News* 15, no. 10 (October 1987): 1, 29.
80. Those subgroups included people with AIDS diagnosed by a bout of *Pneumocystis carinii* pneumonia in the previous four months; people with ARC; people with Kaposi's sarcoma but no history of *Pneumocystis carinii*; and people with severe neurological symptoms. On the basis of such studies, AZT currently is recommended only for people with AIDS as diagnosed by a history of *Pneumocystis carinii* pneumonia and for people with helper T-cell counts below a specified threshold. Still under investigation also are the effects of AZT for infants with AIDS, and the impact of AZT on progression of disease in asymptomatic seropositive patients.

**"T**he PWA does have an integral role to play in this health crisis. But government health agencies and politicians, especially the ones in power, tend not to take PWAs too seriously. Many have never seen a PWA in their life; there may even be people in this room who have never met a PWA in their life. We tend to be a novelty act, and when that novelty wears off, the doors may not open to us anymore. I don't believe the government has ever had to deal with patients' organizations like this before and they simply don't know what to make of us, so they humor us. PWAs are not seriously consulted on decisions that affect our lives and our freedoms. PWAs are always the last to know anything about what the government is doing. **"**

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## **Glossary**

- Etiologic agent.** The cause or source of a disease; in the case of AIDS, the infectious virus.
- Immunosuppression.** Abnormal or depressed ability to maintain immunologic integrity; especially, an inability to fight infection.
- Interferon.** A protein capable of limiting superinfection; produced by cells when infected with a virus.
- Interleukin.** A protein substance produced by white blood cells which regulates the function of other white cells and intracellular virus replication.
- Seroepidemiology.** The prevalence and distribution of antibodies, reflecting the degree and extent of infection of a population.