The Window Period Re-examined: An Update for HIV Counselors
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Introduction

A change in window period recommendations?

Current HIV screening tests are designed to detect antibodies to HIV. Because it takes a period of several weeks or months for these antibodies to develop after exposure, clients testing for HIV are typically advised to test again later if they have recently engaged in risk behavior that may have exposed them to HIV. Previous guidelines recommended retesting six months after the most recent potential exposure. However, a number of states have changed their counseling guidelines to recommend retesting after three months, citing improvements in testing technology for a 50% reduction in the window period (WP). However, an examination of the existing literature revealed no evidence to support this change.

Original estimate: 95% seroconvert in six months

The Office of AIDS recommendation of six months is drawn from a 1989 article estimating the time period from exposure to seroconversion (Horsburgh, Ou et al.). Based on a sample with a known exposure date, Horsburgh estimated that 95% of infected people would seroconvert within 5.8 months of exposure, and about half would seroconvert within two months. This conclusion is consistent with data from health care workers seroconverting after a needlestick incident (Ciesielski & Metler, 1997).

Infectious WP shorter than exposure-to-seroconversion

A review of the subsequent literature examining time to seroconversion revealed that the majority of these studies were concerned with examining the safety of the blood supply. Consequently, this body of research examined the infectious WP – the period of time during which blood would test negative for HIV antibodies but would nonetheless result in HIV infection in the recipient.

Because it takes some time for enough virus to replicate in the body to be infectious to others, the infectious WP is shorter than the time period between exposure and seroconversion (Busch and Satten 1997; Murthy, Henrard et al. 1999). For the purpose of advising HIV counseling and testing clients, it is critical to distinguish between this infectious WP and the longer period between exposure and seroconversion – a period that may more accurately be referred to as the exposure WP.

Confusion around window period estimates?

In an examination of more than 70 studies referenced to support a change in window period recommendations, no definitive study or series of studies emerged. Instead, it appears that the recommendation for a three-month window period may be the result of a failure to distinguish between these two window periods.

Definitions

In order to understand the important distinction between the two window periods, the following definitions may be useful:

Exposure event
The event that potentially exposed a client to HIV; e.g., sex or needle-sharing with a partner who may be HIV infected, etc.

Exposure Window Period
The period of time between the exposure event and seroconversion. It is important to accurately estimate this interval in order to establish effective recommendations regarding the retesting interval for clients who may have been exposed to HIV.

Eclipse period
The period of time after exposure but before virus has replicated enough to be infectious.

Infectious Window Period
The period of time between infectious viral load and seroconversion. During this time someone who is seroconverting will test negative for HIV antibodies but may still infect a sexual or needle-sharing partner or blood recipient. The length of this interval is important for estimating the safety of the blood supply.

Seroconversion
The point at which HIV antibodies reach levels that are detectable by current HIV tests. At this point, the client will test positive for HIV.
The Process

For the purposes of HIV counseling and testing clients, the exposure window period begins at the most recent possible exposure event – that is, the last time the client engaged in behavior which may have put him or her at risk for HIV.

During the “eclipse” period, the virus in an infected client begins replicating in submucosal cells, which subsequently travel to lymph nodes. At this point the virus is not circulated in the blood stream, and is not detectable. The client is not yet infectious. The length of this period may be affected by the amount and virulence of the viral strain, the functioning of the immune system, the mode of transmission, etc. It appears to be highly variable from one person to the next.

After the virus enters circulation, there is a period of viral “ramp-up.” During this time the virus replicates quickly. When viral load reaches sufficient levels, the person becomes infectious.

In response to increasing viral loads, the immune system creates HIV antibodies. Pre-seroconversion symptoms are believed to be a result of this immune response. When enough antibodies are formed, they become detectable by current HIV antibody tests. This marks seroconversion.

The Evidence

An examination of the research cited to support a three-month exposure WP revealed no conclusive evidence for such a change. Most studies cited fell into one of the categories below:

- The cited study actually referred to the infectious WP rather than the exposure WP.
- The Horsburgh study was cited, but the original source incorrectly indicated that this study provided evidence of a three-month exposure WP.
- The reference cited a series of case studies in which some or all of the subjects seroconvert within two to three months, but most also acknowledged “exceptional” cases in which seroconversion took longer.
- The reference cited a study in which symptomatic seroconverters report an exposure incident during the previous three months, but it is not clear whether there were earlier exposures within the prior six months.

The critical point is that after following up more than 70 studies referenced in regard to a three-month exposure WP, no definitive study or series of studies which supports a three-month reduction in the Horsburgh estimate has emerged. While it is possible that the Horsburgh estimate may have been inaccurate to begin with, it remains the most definitive study to date that systematically estimates the period from exposure to seroconversion.
Sources of Confusion

Several factors may have contributed to the apparent confusion between the infectious WP and the exposure WP.

An initial assumption that the infectious WP and exposure WP were virtually the same

“…we assume that the PCR-positive, antibody negative period is essentially the same as the period from infection to seroconversion” (Horsburgh et al., 1989, p. 637). There is now substantial evidence for a significant period of time after exposure and prior to infectiousness (Busch and Satten 1997; Murthy, Henrard et al. 1999), which has been termed the “eclipse” period (Busch and Satten, 1997).

Lack of distinction in terminology

Researchers concerned about the safety of the blood supply conduct investigations to determine the duration of the infectious WP. Within the context of such research, this period is frequently referred to as simply the “window period.” Unfortunately, this is also the only term in common usage to describe the time between exposure and seroconversion.

Infectious WP reduced by about 50%

Current HIV tests can now detect HIV antibodies about 23 days sooner than first generation tests. The effect is that the infectious WP has been reduced from 45 days to 22 days, a reduction of about 50%. Because the infectious WP is often referred to as simply the “window period” in these reports, readers may have erroneously concluded that the exposure window period had been reduced by 50%, from six months to three months.

No Change to OA Recommendations

Although future research may shed more light on the exact process and duration of the exposure window period, the original Horsburgh estimate adjusted for technological improvements may be the best estimate currently available. This revised estimate suggests that 95% of those seroconverting will do so within about five months of the exposure event, and about half will do so within five weeks. Because this is a relatively minor revision to the original estimate, the Office of AIDS will continue to recommend retesting six months after a potential exposure to rule out HIV infection.

What the Client Needs to Know

Although its important for health care providers – especially HIV counselors – to avoid confusing the infectious window period and the exposure window period, it is not critical for the client to understand this distinction. Clients simply need to be aware of the following issues:

1. Because many people who are infected will seroconvert within two to three months, it may be useful to be tested two to three months after an isolated exposure event, to “rule in” infection and receive early care.

2. Clients testing negative two to three months after an isolated exposure event must retest six months after exposure to “rule out” infection.

3. For clients in the six-month window period, there is a period of time prior to seroconversion when they may be infectious to others, in spite of testing negative for HIV antibodies.

Conclusions

Understanding the duration of the exposure window period is crucial for health care providers to accurately inform clients at risk for HIV. Future research must focus on clarifying this issue in order to provide the most clear and accurate information possible, in the interests of public health.

References


