

## HIV testing in COVID-19 pandemic and beyond in Japan

Shinichi Oka\*

AIDS Clinical Center, National Center for Global Health and Medicine, Tokyo, Japan.

**Abstract:** In Japan, HIV testing has been offered anonymously and free-of-charge at local public health centers, together with pre- and post-test counseling since 1993. Since then, the number of HIV tests increased steadily to reach a peak in 2008 but has since decreased by 30% during the last decade. The number of tests further decreased in 2020 during the COVID-19 pandemic and steeply by 50% this year compared with the previous year, mostly due to a shift in the workload at these centers to COVID-19-related services. To deal with this decline and thinking beyond the current pandemic, more options for HIV testing are needed, such as self-testing/postal delivery of dried blood spot specimen, a method that is yet to be approved in Japan, in addition to the conventional plasma/serum-based HIV testing.

**Keywords:** HIV testing, COVID-19 pandemic, self-testing, dried blood spot, postal service

The standard HIV testing protocol in Japan consists of two consecutive reactive tests to confirm an HIV positive diagnosis (1). It recommends the use of the 4th generation HIV-1/2 antigen-antibody screening assay followed by another HIV-1/2 antibody confirmatory assay and/or nucleic acid amplification test (NAAT) to detect HIV in serum or plasma specimens. This protocol is employed at laboratories in medical facilities or local public health centers across Japan. At medical facilities, all high-risk individuals (defined as those with incident sexually transmitted infections and multiple sexual partners) should undergo screening for HIV infection. However, many patients with undiagnosed HIV infections are seen several times at medical facilities before they actually undergo HIV testing. In other words, physician-directed testing is not always efficient.

Another opportunity is voluntary testing at local public health centers. Testing at these centers is strongly recommended because it is free of charge, anonymous, and bundled with pre- and post-test counseling. In Japan, such centers have served as voluntary counseling and testing centers for HIV since 1993. The number of HIV tests conducted at such centers reached a peak (at 177,000) in 2008. Admittedly, some of these centers are not always convenient, for example, operating only one hour a week, closed over weekends, requiring appointments, or multiple visits (one for testing and another for results). Therefore, the number of such tests fell by 30% in the last decade (2). More importantly, the number of tests conducted in 2020 decreased precipitously by around 50% compared with the previous year (from 142,000 in 2019 to 69,000 in 2020) (2) mainly due to the shift in the workload at these centers towards providing COVID-19-related services. To counter this

fall in HIV testing, it is important to design alternative methods for HIV testing that can be executed without the need to visit the local public health centers.

The number of self-collected dried blood spot (DBS) test cards delivered by postal service has been increasing steadily in the last two decades, and probably now outnumbers the tests conducted at the local public health centers. The estimated number of such tests is more than 100,000 per year, although the exact number is unknown. The advantages of HIV testing using mail-posted-DBS include simple and easy self-preparation of finger-prick-blood spots at ambient temperature that can be posted 24 hours a day/7 days a week throughout the year. Therefore, people would not need to visit medical facilities or local public health centers. However, DBS is not yet approved as a clinical sample for HIV testing in Japan. In this regard, even in the US, only a limited number of commercial DBS-based test kits have been approved so far by the Food and Drug Administration (FDA) (3). To use DBS widely, we have to elucidate its applicability for HIV testing, and current studies are very limited (4). According to our data, DBS sample is around 200 times more dilute because a small amount of whole blood on filter paper is eluted with phosphate buffered saline. Therefore, HIV testing with DBS is estimated to be less sensitive than with a plasma sample. Notably, however, the antibody titers are continuously changing over time (5) and testing with DBS can detect many HIV patients with enough sensitivity and specificity, excluding those with acute infection. In this context, our previous outreach study (6) confirmed the high successful rate of HIV testing with self-collected postal service-delivered DBS in Japanese men who have sex with men (MSM) (representing a high-risk population).

DBS seems feasible and reliable.

When we look at the world, the importance of HIV testing has been considerably recognized in the last two decades and there are currently many options. Advances and innovation in medical technology have helped spread the use of HIV testing in both the developed and developing countries in terms of clinical specimens (e.g., oral fluid or DBS), testing protocols (e.g., self-testing or using postal service), and access to testing (e.g., collaboration with groups or social networking). For maximum reduction in the number of new cases of HIV infection with a goal of "Ending the HIV Epidemic", we have to identify all HIV infected people who are not yet diagnosed, start antiretroviral therapy (ART) as early as possible, and ensure that the viral loads are maintained below the detection levels, based on the scientific concept of "Undetectable equals Untransmittable (U = U)" (7). HIV testing is the gateway to a series of steps for expansion of ART coverage. The WHO recently issued innovative HIV testing recommendations in response to contemporary needs (8). The US Center for Disease Control (CDC) also recommends repeated HIV testing of key populations, preferably every 3 to 6 months for early assessment of HIV status (9). Furthermore, HIV pre-exposure prophylaxis (PrEP) has been offered to high-risk populations worldwide in this decade and a recent study confirmed that PrEP successfully prevents HIV infection in the long term (10). People on PrEP are strongly recommended to undergo quarterly HIV testing. Under these circumstances, self-testing using home collection kits or oral swab-based tests should be considered, especially when facility-based services or in-person contact is limited (11). Another step towards achieving "Ending the HIV Epidemic" would be the simultaneous implementation of both ART to patients and PrEP to high-risk populations.

Looking back and thinking ahead of the post-COVID-19 pandemic in Japan, we need more "user-friendly" options for HIV testing that allow self-testing, including the use of DBS or oral-swabs as an alternative to plasma or serum specimens. HIV testing should be positioned as the first step to reducing new HIV infections. This should be used in conjunction with early ART after diagnosis and PrEP for at-risk populations. Otherwise, we will have to deal with the more serious situation of HIV endemic in the future.

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**\*Address correspondence to:**

Shinichi Oka, AIDS Clinical Center, National Center for Global Health and Medicine, 1-21-1, Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.

E-mail: [oka@acc.ncgm.go.jp](mailto:oka@acc.ncgm.go.jp)