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A Primer in HIV Testing

by Dr. Adele Visser

Introduction

By the end of 2021, an estimated 38,4 million people were living with the human immunodeficiency virus (HIV-1) worldwide of which two thirds are living in the African region.

In 2021, more than half a million people died from HIV-1 and 1,5 million newly acquired the virus[1].

HIV-1 infection will remain a major contributor of morbidity and mortality in our health care sector until an effective cure and / or prevention is produced.

For this reason, we need to understand when and how to utilize the laboratory assays available to us, both in the diagnostic and the monitoring sector.

Basic virus pathophysiology as it impacts on testing It is imperative to understand the lifecycle of the HIV-1 virus to fully understand in which settings certain tests can be used (figure 1).

Laboratory Testing for HIV

There are three major avenues of HIV-1 testing, each with specific indications (table 1).

Serological testing uses either blood, serum or saliva for the detection of antigens directly from the virus and antibodies as produced by the body against the virus.

Figure 1. HIV Life Cycle Viral replication and sites where testing is targeted.

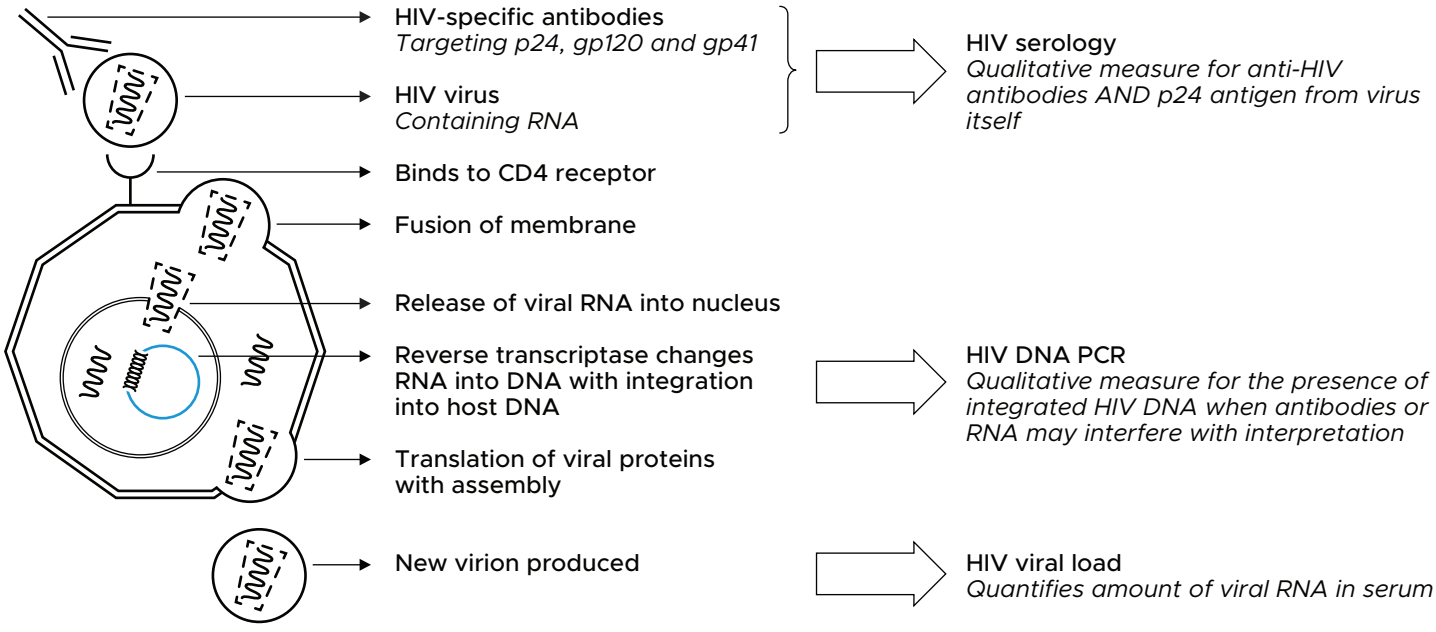

Table 1. Testing modalities in the diagnosis of HIV-1 and their clinical application.

Testing Focus		Clinical Application
HIV-1 serology in blood, serum or saliva.	Rapid	Used in the diagnosis of patients ≥18 months of age. Requires confirmation.
	Laboratory	Used in the diagnosis of patients ≥18 months of age.
HIV-1 RNA PCR *(viral load)*.		Monitoring the effectiveness of antiretroviral therapy.
HIV-1 DNA PCR.		Diagnosis of HIV in children <18 months of age *Serology may give false positive result as maternal antibodies may persist*.

Of note, the laboratory assays typically do not distinguish between which of these are positive, once a reactive test is acquired.

The combination of both antigens and antibodies, which came to be referred to as the 4th generation assays, hold the advantage of a shorter window period of detection. In most instances, the presence of antibodies indicate infection with the virus, with the exception of maternal antibodies present in the infant. In these cases, the virus needs to be demonstrated directly. For this reason, a HIV-1 DNA PCR is the test of choice, to demonstrate the presence of integrated virus.

Indeterminate or Invalid Results

In certain cases, the HIV-1 serological assays show a weak positive reaction, not at a high enough threshold to be considered as positive.

In these instances, the test is reported as invalid or indeterminate.

This scenario may be due to a host of causes, including but not limited to recent infection with HIV, cross-reaction with other antibodies or various technical issues.

Although rare, this is a well described clinical situation, which should be managed by counselling of the patient, and follow up testing after a waiting period. Due to the distress caused to the patient in these settings, the shortest period of 2 weeks is advocated[2].

If the test remains indeterminate, the case should be discussed with a pathologist who will advise of the most appropriate course of action.

References

1. https://www.who.int/news-room/fact-sheets/detail/hiv-aids
2. https://www.aidsmap.com/about-hiv/faq/what-does-indeterminate-mean-when-testing-hiv

JDJ Pathology Laboratories

☎ 031 201 4647
067 826 7473
031 201 4910
clientservices@jdjd.co.za
accounts@jdjd.co.za
www.jdjd.co.za