Point of care using simple/rapid HIV tests

Kate Learmonth
Dale McPhee &
Elizabeth M Dax

National Serology Reference Laboratory (NRL), Australia*
4th Floor, Healy Building
41 Victoria Parade, Fitzroy VIC 3065
and
Departments of Microbiology and Immunology and Medicine at St Vincent's
The University of Melbourne
Tel: (03) 9418 1111
Fax: (03) 9418 1155
E-mail: liz@nrl.gov.au
*The NRL is a WHO Collaborating Centre on HIV/AIDS

Movement of HIV testing to point of care (POC) has been facilitated by the availability of simple/rapid anti-HIV immunoassays. These assays have been used at health centres in the United States, Canada and at voluntary counselling and testing centres in developing countries (Figure 1). While this approach has revolutionised HIV screening in some areas, there are ethical, legal and quality assurance considerations that must be addressed before POC HIV testing is universally accepted.

In 1983, HIV was identified as the virus leading to AIDS [1]. Since then, HIV has spread to all continents and is pandemic. In 2005 an estimated 40.3 million people were infected worldwide [2]. The majority (25.4 million) of those infections were in Sub-Saharan Africa, where lack of infrastructure has fuelled a high incidence of infection [2].

The continuing high rate of spread of HIV is principally due to its unusual pathogenesis which incorporates a long latency period, during which people may be unaware of their infective status. High-risk activities such as unsafe sex with multiple partners (heterosexual and homosexual) and injection drug use have contributed to the spread of HIV. This has resulted in rapid increases in infection rates being observed in China, India, Thailand and Cambodia [2]. The majority

Figure 1. An example of a situation of POC testing in Vietnam (Photo – Liz Dax).

of the 4.9 million new infections in 2005 were heterosexually transmitted [2].

To combat the growing pandemic, international initiatives such as the Global Fund [to fight] AIDS, TB and Malaria (GFATM), the US-run President's Emergency Plan for AIDS relief (PEPFAR) and the UNAIDS/WHO '3 by 5' initiative (aimed to treat 3 million HIV infected people with antiretrovirals by the end of 2005), have been implemented. Prevention through education, wider testing with informed consent and treatment via universal access to antiretrovirals is foremost on their agendas. The use of simple/rapid HIV tests (RTs) as POC tests and the impact this has on HIV control is crucial in achieving these agendas.

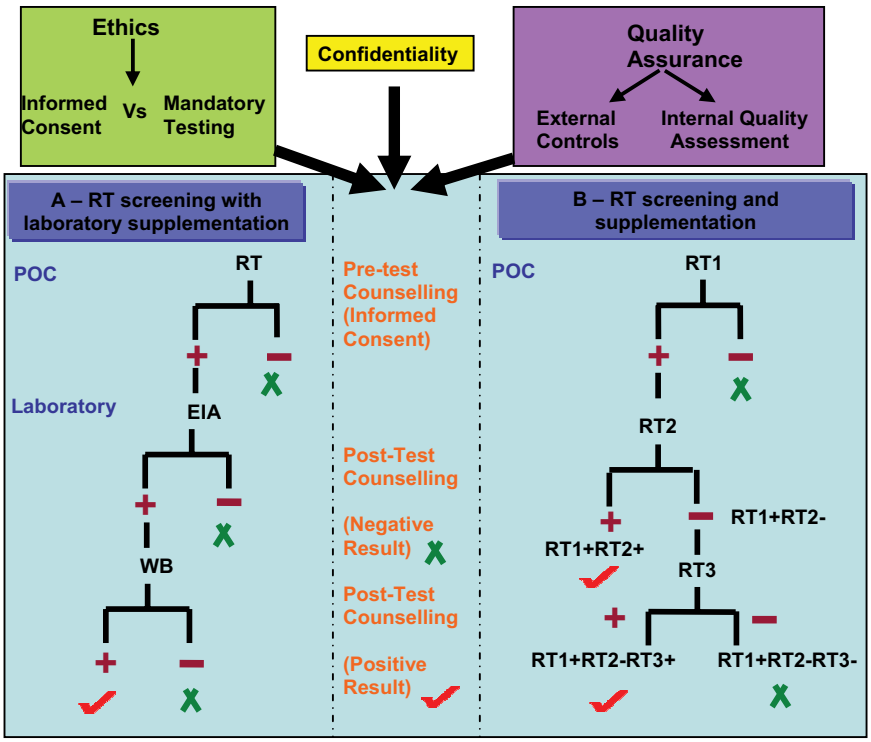

Figure 2. HIV diagnostic testing algorithm using simple/rapid HIV tests.
Ethics, confidentiality and quality assurance are all important factors in successful HIV testing. Pre-test counselling guides informed consent, while post-test counselling focuses on the client's need. If a negative HIV result is found, a prevention and risk assessment is conducted. If the result is positive, then counselling allows the client to understand what this means and if possible to organise a treatment regime.
A:RT at POC with laboratory follow up of reactive RT with an enzyme immunoassay (EIA) and a western blot (WB) if the EIA is reactive to confirm diagnosis. A non-reactive RT signifies a negative HIV result. This algorithm is used predominantly in well-resourced countries.
B: RT at POC used in sequence to confirm diagnosis. A reactive RT result indicates that a second, complementary RT is used. If the results are discordant, then a third RT is used. This algorithm is based on the UNAIDS and WHO strategy III for RT testing [12] and is predominantly used in resource-limited settings.

Simple/rapid HIV tests (RTs)

RTs detect antibodies to HIV-1 and/or HIV-2 from blood, plasma or serum. They are presented as single use agglutination, immunochromatography, immunofiltration or immunodot assays typically performed with a finger-prick blood sample. When used in a quality-assured manner they are as good as, and in some situations potentially better than, conventional enzyme immunoassays, with specificities and sensitivities approaching 100% [3]. These tests are easy to use, can be performed and read with only basic technical training and without the need for specialised equipment. They do not require utilities, which make them ideal for use at POC in developing countries.

They are also potentially useful in determining serostatus in 'emergency situations' such as in the emergency room, during labour (to determine maternal HIV serostatus, thereby potentially preventing vertical transmission) and in assessing the need for antiretrovirals after an occupational exposure.

Most importantly, and unlike other expensive immunoassays and nucleic acid testing conducted in laboratories, they take less than 30 minutes from when a blood sample is taken to the clients receiving a negative result. If the result is reactive, in Australia and the US the sample is then retested using a conventional testing algorithm in a laboratory (Figure 2). Currently, for HIV testing, blood is sent to a laboratory and clients must return later to receive their results. In the US, 2.3 of 17 million people tested for HIV between 1994 and 1995 did not collect their results [4]. Therefore, the ability of HIV RTs to provide results at POC potentially alleviates this situation.

POC testing and RTs

POC testing refers to "testing performed outside a central laboratory environment", usually by a qualified health care worker [5]. All HIV testing should follow algorithms in which a reactive screening test is followed by supplemental testing to distinguish true- from false-positive reactivity and confirm the HIV serostatus. Counselling by a qualified person is part of the policy in Australia and is recommended by the WHO [3]. These sessions should include basic education on prevention and risk assessment [3].

In Australia, RTs are presently limited to use in forensic testing and reference laboratories as supplemental assays. The results must be followed up in a laboratory-based algorithm. When used in a POC setting, RTs will be performed by a health care worker.

There are significant differences in the ways developed countries and developing countries may use RTs at POC. In developed countries, if an RT result were reactive, the sample is sent to a laboratory for confirmation using a conventional testing strategy. Developing countries often follow the recommended WHO testing strategies and use RTs. If two RTs are reactive at the POC, the client will be given a positive HIV diagnosis, usually with accurate results.

Quality assurance of RTs

The selection of RTs per the WHO evaluations [6] should be based on performance, availability, shelf-life, storage requirements and cost [3]. It is imperative that sequential tests complement each other with regard to identifying falsely reactive results and that these are used within the limitations specified.

The WHO has evaluated numbers of RTs [6]. They recommend that tests are evaluated in the population of their intended use and emphasise the importance of employing stringent internal and external controls [3]. The importance of quality controls was highlighted by a case in Canada where an RT was recalled after it was found to have inadequate sensitivity [7]. It has been shown that certain HIV-1 subtypes, seroconversion and antiretroviral use may generate erroneous results, further emphasising the need for quality assurance both before and while tests are in use [7, 8].

Ethical and legal considerations

Most guiding bodies, including the WHO and the Australian government, advocate that all HIV testing should be voluntary, confidential and conducted with informed consent [3]. The introduction of RTs into POC settings has led to concerns that protection of confidentiality may be inadequate, especially in emergency situations where voluntary consent may be compromised or impossible [9].

Another concern is mandatory testing. While screening of a whole population has not yet been implemented in any country, it has been considered in some African countries to help curb transmission rates [10]. There is also concern that employers may insist on HIV testing, leading to discrimination against HIV positive people. An example was the forced screening of employees by a Zambian mining company in 2001 [11]. Most nations have decided upon an 'opt-in' or 'opt-out' HIV screening policy. Effective government policy around HIV testing especially at POC is therefore imperative. While guidelines can be issued, e.g. by WHO, it is up to each government to implement them [12].

Conclusion

The implementation of RTs at POC offers significant advantages in assisting in the control of the spread of HIV. By increasing the knowledge of serostatus among high-risk populations by using POC HIV testing in satisfactorily quality managed testing strategies, transmission rates may be lowered. While there are still major concerns and the possibility that RTs may be misused, the main question is whether the benefits outweigh the concerns.

Acknowledgements

Thanks to Dr Kim Wilson for her thoughts and editing skills.

References

1. Barre-Sinoussi F, Chermann JC, Rey F *et al.* Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983; 220:868-71.
2. UNAIDS. *2005 Report on the Global AIDS Epidemic.* 2005.
3. WHO. *Rapid HIV Tests: Guidelines for Use in HIV Testing and Counselling Services in Resource-Constrained Settings.* 2004.
4. Tao G, Branson BM, Kassler WJ & Cohen RA. Rates of receiving HIV test results: data from the US National Health Interview Survey for 1994 and 1995. *J Acquir Immune Defic Syndr* 1999; 22:395-400.
5. Commonwealth of Australia, http://www.health.gov.au/internet/wcms/publishing.nsf/content/health-pathology-poctt-index.htm/$file/poct_standards_and_guidelines.rtf. *Standard for Point of Care Testing in General Practice.* November, 2004.
6. WHO, UNAIDS. *HIV Assays: Operational Characteristics Report 14/ Simple/Rapid Tests.* 2004.
7. Rekart ML, Krajden M, Cook D *et al.* Problems with the fast-check HIV rapid test kits. *CMAJ* 2002;167:119.
8. Makuwa M, Souquiere S, Niangui MT *et al.* Reliability of rapid diagnostic tests for HIV variant infection. *J Virol Methods* 2002;103:183-90.
9. Elliott R & Jurgens R. Rapid HIV screening at the point of care: legal and ethical questions. http://www.aidslaw.ca/Maincontent/issues/testing/finalreports/graphics/e-rapid.pdf: *Canadian HIV/AIDS Legal Network.* 2000.
10. Noble R (accessed 27/02/06). *HIV AIDS in Zambia: Prevention and Care:* ©AVERT 2005.
11. Mwanangombe L. http://www.medguide.org.zm/aids/aidszam31.htm#produces. Controversial Testing Produces Unexpected Results. *Panafrican News Agency.* 2001.
12. WHO, UNAIDS, CDC, USAIDS. *Guidelines for Using HIV Testing Strategies in Surveillance: Selection, Evaluation and Implementation.* 2001.