AIDS FORUM

Laboratory monitoring of HIV/AIDS in a resource-poor setting

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Currently less than about 5% of individuals requiring anti-retroviral therapy (ART) can access these medicines in a resource-poor setting. In South Africa there are at least 4.7 million HIV-positive individuals, each of whom has a right to therapy. Access to ART has, however, been limited locally to that minority of individuals fortunate enough either to be able to afford to pay independently, or to have entered sponsored programmes of HIV / AIDS disease management. Sponsorship may be related to pharmaceutical drug trials, grant-funded programmes, or HIV / AIDS programmes offered by employers. To parallel ART initiatives, laboratory monitoring of varying degrees is essential to ensure that safety is not compromised in individuals taking ART drugs. Despite recent substantial decreases in ART costs (in some instances free drugs), expensive laboratory testing may still be a limiting factor in the implementation of ART programmes.

Laboratory monitoring of HIV / AIDS could potentially represent a significant challenge to any Third World country, where the total cost of disease monitoring may exceed an annual health budget. Most developing countries are grossly under-resourced, with annual health expenditure per capita frequently less than the current cost of a single viral load assay. The monitoring algorithms utilised for HIV management based on international guidelines[1] are regarded by some as an 'overkill' and inappropriate for use in our local setting.[2,3] Although local innovation offers new hope[4] of bringing down costs of laboratory monitoring, viral load testing remains expensive and inaccessible. Handouts will always be gratefully received for reduced manufacturing costs of reagents,[5] but implementation of sustainable laboratory monitoring and ART programmes will only come with further innovation and creative collaborative efforts. This is the only way forward to manage the HIV / AIDS epidemic in this country.

Many obstacles are noted in the provision of affordable and accessible laboratory monitoring for HIV / AIDS in a resource-poor setting. These include lack of or poor laboratory infrastructure, absence of technical skill, and more specifically, absence of or poor laboratory management skills. Reagent costs are generally high and large capital outlay costs for sophisticated equipment are required. The recent devaluation of the Rand further compounds the problem of dramatically escalating costs of imported equipment, reagents and consumables. There is also frequently poor supplier support in remote areas. Lastly, the restricted use of intellectual property may prohibit use of specific technologies, or specifically, modifications of the technologies, for use in a resource-poor setting.

Detailed costs pertaining to running and management of laboratories are typically underestimated and frequently overlooked. Careful evaluation of relevant infrastructure including related costs such as staff salaries, laboratory rentals, equipment maintenance and sample shipping costs, as well as costs of reagents and consumables, is required to ensure a sustainable laboratory infrastructure. Logistics of sample collection and delivery of results are also very difficult, especially in remote areas. Different laboratories have different needs, which need to be taken into account with regard to the specific environment. Monitoring in resource-poor settings may further require significant modification of internationally recommended guidelines. In some instances, writing of relevant local guidelines may be more appropriate. The novel use of available technology or innovative new technologies and the establishment of affordable, effective quality control programmes are also required. Facilitating informed decision making for implementation of the appropriate technology is therefore essential. This should be based on local technical skills, laboratory resources, volumes of work, availability of

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quality control initiatives and good training programmes.

A single solution in all regions is therefore not feasible and a tiered laboratory approach is the most practical for rapid implementation and affordability, with primary centres preparing and referring more specialised testing to secondary or tertiary testing facilities (both private and public).

Secondary (or in some cases, primary) care centres may develop the capacity to perform less sophisticated testing such as basic chemistry and haematological analysis. In certain instances they may utilise simple systems for CD4 enumeration such as the manual CD4 counting bead assays (Cytospheres; Beckman Coulter, Fla, USA, and Dynabeads; DYNAL, NY, USA). Tertiary academic complexes and major hubs of the private laboratories generally have the ability to perform tests (or at least have the capacity to develop such tests), including flow cytometric-based CD4 tests, nucleic acid amplification techniques for viral load testing, and drug resistance and toxicity screening.

Monitoring generally includes investigations to determine efficacy, toxicity and therapy compliance. A great deal of debate currently centres on how permissive antiretroviral treatment and laboratory-monitoring strategies can be without compromising safety. Several questions need addressing. Can clinical parameters such as weight gain, quality of life assessment or a reduction in complications replace laboratory monitoring? Are there less expensive surrogate markers? Can laboratory testing be performed less frequently? Many of these issues are addressed in the new draft World Health Organisation guidelines entitled 'Guide to ART in resource limited settings' (**http://www.who.int/HIV_AIDS/WHO_HSI_2000.04_1.04/003. htm**). This document further defines two related but different dilemmas: the need to distinguish between an overall public health perspective for wide-scale implementation of ART versus individual patient management. The document outlines the use of laboratory investigations, divided into four categories: (*i*) absolute minimum tests; (*ii*) basic recommended tests; (*iii*) desirable tests; and (*iv*) optional, tests (**http://www.who.int/hiv/topics/arv/scaling_exe_summary.pdf**). In this guideline, a consensus was reached that the absolute minimum requirements for initiation of therapy should include an HIV antibody test and a haemoglobin and / or haematocrit level. Basic recommended testing should include a white cell count and differential count, basic liver function assays including AST and ALT (to monitor for co-infection with hepatitis or drug-related hepatotoxicity), serum creatinine / urea, serum glucose, and pregnancy tests for women. Expanded liver function profiles (including amylase, bilirubin and lipids) and CD4 testing are considered desirable tests. Viral load testing is considered an optional test because of high associated costs.

Although our funding is limited, the outlook for monitoring in South Africa appears favourable. There is a well-developed laboratory network comprised of both the private sector and the newly formed umbrella national laboratory service, viz. the National HealthLaboratory Service (made up of existing provincial and academic hospital-based facilities, the erstwhile South African Institute for Medical Research laboratories and other centres of excellence, e.g. the National Institute of Virology). Centres with poor or no infrastructure for collection of samples and delivery of results are being revitalised by using off-road motorcycles for specimen collection, and an SMS reporting system using the existing well-developed GSM (cell phone) wireless networks. This local innovative concept introduced into certain areas of the Transkei has revolutionised a previously severely limited Transkei laboratory infrastructure, enabling remote clinics access to a laboratory service. Requests for collection of samples can be communicated by SMS, and facilitated by the use of off-road motorbikes that collect the samples in remote sites and deliver them to local laboratories. Individual patient results are sent back at very low costs via SMS to the requesting clinic sister (web link: **www.exactmobile.com/Press/PressResults.asp?ID=32**). This system can be further enhanced by use of interactive WAP (Wireless Application Protocol) or more powerfully by the recently introduced General Packet Radio Service (GPRS) standard, which will allow ultra-fast data transfer via a continuously connected pipeline in a 'pay per bit' system. In fact this latter technology holds considerable promise for viable implementation of many of the existing telemedicine applications that previously failed because of their reliance on telephone landlines and expensive, proprietary hardware and software.

In conclusion, there are several centres of excellence across the country, and it is unlikely that South Africa will lack the laboratory capacity to support national rollout of ART. There are at last 20 flow cytometry facilities across South Africa and numerous molecular laboratories to support a national treatment plan. The high cost of reagents still needs to be addressed. Although some local initiatives are in place to provide very affordable 'generic' monoclonal antibodies[6] for CD4 testing to contain costs in the state sector, further initiatives are still needed to entice manufacturing companies and other manufacturers of testing components to reduce the costs of reagents required for testing, especially those of viral load.

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