The Battle against Infectious Diseases in Developing Countries: The Inseparable Twins of Diagnosis and Therapy

The lack of treatment of infectious diseases in developing countries is a tragic problem and one of the most serious challenges that the world must face at the beginning of this century. Hundreds of millions of people suffer from transmissible diseases for which treatments exist but for which the patients are not receiving treatment. The case of HIV infection is symbolic: the vast majority of patients are living in countries where access to treatment is difficult, incomplete, or impossible.

The problem of access to treatment has been discussed frequently. By contrast, its crucial connections with the problem of diagnosis are rarely enunciated. However, identification of the etiology of an infectious disease and monitoring of the infection during therapy are required for effective and efficient treatment.

In this issue of *Clinical Chemistry*, Drosten et al. (1) describe a new method based on real-time reverse transcription-PCR for the monitoring of HIV-1 viral load. An important concern is the genetic diversity of HIV-1 worldwide and the continued evolution of the virus. Hence, quantification of HIV-1 genome RNA in plasma presents an ongoing challenge. Since 1999 (2), several real-time PCR protocols have been proposed. Real-time PCR assays that can be developed within the laboratory are attractive for monitoring HIV-1 viremia in resource-limited settings because of their robustness, speed, and simplicity and their low cost, large dynamic range, and reduced contamination risk compared with traditional end-point assays. In one example, Rouet et al. (3) showed that they could transfer an automated low-cost real-time reverse transcription-PCR protocol for routine use in West Africa.

The approach described by Drosten et al. (1) merits special attention, however. As proposed in previous studies (3–5), Dr. Drosten and collaborators designed an amplification test targeting the 5′ long terminal repeat domain of HIV-1. What is proposed here is not only a low-cost procedure. The authors have built a complete, sophisticated, robust protocol that, in terms of sensitivity, spectrum of virus variants detected, and quality control, can compete with (or surpass) the widely used methods that are commercially available in developed countries. The analytical sensitivity of the assay allows a broad quantification range (50 to 10 000 000 IU/mL), and the test provides reliable quantification not only for HIV-1 subtype B (the most frequent in western countries) but also for non-B subtypes (more frequent in sub-Saharan Africa and Asia) and N/O variants. This is not the case for other methods that are based on amplification of the gag gene and that often have been optimized for the amplification of HIV-1 subtype B. In addition, the authors’ efforts in the production of calibrators and controls and in the evaluation of test performance reach a level that is at least as high as that for commercially available methods used in developed countries.

The publication of this method provides concrete evidence that affordable, nonpatented, ultrasensitive HIV-1 viral load assays appear feasible in countries where monitoring of viremia could not be envisaged previously for financial reasons. As underlined by the authors, in some countries, “monitoring of antiretroviral therapy is now more expensive than treatment itself” (1). Collaboration by scientists from South Africa, India, and Brazil, all countries with efforts to make available efficient antiretroviral therapy, reflects the medical, economic, and political issues of access to low-cost diagnostic tests. Because monitoring of HIV-1 viremia is clearly a key for the management of antiviral therapy (including drug resistance and mother-to-child transmission diagnosis), the potential benefit of the method proposed here is enormous in terms of public health.

Finally, this work also illustrates the unique potential of real-time methods for development of low-cost, standardized diagnostic tests that do not require specific costly equipment. The procedure used by Dr. Drosten and collaborators (1) for designing and validating their HIV-1 assay may be used as a convenient model for elaborating comparable tests for other human pathogens.

References


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DOI: 10.1373/clinchem.2006.071316

*Clinical Chemistry* 52, No. 7, 2006 1217