Eur. J. Clin. Chem. Clin. Biochem.
Vol. 29, 1991, pp. 331–337

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Berlin · New York

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Comparison of Four Anti-HIV Screening Assays Which Belong to Different Test Generations

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(Received September 6/December 22, 1990)

Summary: There are three different test generations of enzyme-linked immunosorbent assays (ELISA) for the detection of human immunodeficiency virus (HIV) infection, depending on whether virus lysate, recombinant proteins or synthetic peptides are used as solid phase antigen. Four different assays, i.e., three sandwich ELISAs and one competitive test, were used to demonstrate differences between the three systems with regard to the content of different diagnostically relevant virus proteins. The sensitivities and specificities of these assays were compared by using 312 anti-HIV positive sera and 500 sera of healthy blood donors. The highest sensitivity and specificity were achieved by the competitive ELISA based on recombinant proteins, and by the sandwich ELISA based on synthetic peptides.

Introduction

The most common screening method for the diagnosis of infection with human immunodeficiency virus (HIV) is the detection of virus-specific antibodies by sandwich ELISA. There are three different test generations, which differ with respect to the insolubilized antigen used:

The assays of the first generation are based on the adsorption of purified lysed virus cultivated in immortalized human lymphocytes. The quantitative ratios between the virus proteins are difficult to reproduce from one preparation to the other. In addition, diagnostically relevant virus proteins, such as env-gene-derived products, are often not available in sufficient quantities (1). On the other hand, host cell proteins incorporated in the virus membrane cannot, or can only incompletely, be removed (2). Antibodies to HLA-DR antigens may therefore produce false-positive results (3), especially in patients with autoimmune disorders or in multiparae (4). The sensitivity of these tests ranges from 97.2% to 100%, their specificity from 70% to 100% (5).

To circumvent these problems, the assays of the second generation use recombinant proteins as antigen. The composition of the antigen used for insolubilization is now reproducible and can be selected according to the diagnostic relevance of the virus proteins. These proteins, however, require an extensive purification to avoid false positive reactions.

Synthetic peptides used as antigens in third generation tests permit the binding of exclusively specific immunodominant sequences to the solid phase. The reduction of a great number of reactive epitopes of the virus to a few or just one sequence requires a detailed epitope mapping (6). The peptide used in the test has to represent a region, which

(i) induces an antibody response in all HIV-infected persons,

(ii) provokes an antibody response as early as possible,

(iii) maintains the antibody response over all the stages of the disease (7).