
HIV ANTIBODY TESTING METHODS 1985-1988

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The first HIV antibody screening assays were licensed by the Food and Drug Administration (FDA) in March of 1985. By late summer of 1985 the insurance industry had begun to utilize these test to assess an individual's risk of developing AIDS. At this point the etiological agent responsible for the disease was thought to be part of a family of viruses known as the Human T-Lymphotropic Virus and was called HTLV-III. It was later named Human Immuno-deficiency Virus (HIV).

The licensed Enzyme-Linked ImmunoSorbant Assay (ELISA, or Enzyme Immuno-Assays, EIA) was the result of an intense effort to develop tests that could be used to protect the nation's blood supply and, therefore, reduce the spread of disease by this mode. For this reason the tests were designed to be very sensitive. Very little emphasis was given to test specificity. The protocol recommended by the HIV antibody ELISA manufacturer consisted of initial ELISA screening followed by repeat ELISA testing, in duplicate, for all samples found to be initially reactive. Specimens found to be repeatedly reactive with the ELISA screen would require supplemental confirmatory testing. This was typically accomplished by western blot analysis.

Between 1985 and October 1987, western blots utilized for the insurance industry were being performed by one of several means: "home brew" methods, outside reference laboratory testing commonly offered by the ELISA

assay manufacturer, or more commonly, with non-licensed western blot kits. The latter method was most attractive because of the high degree of variability associated with "home brew" methods and the lengthy turnaround time requirements of outside reference lab testing. Western blot banding patterns were primarily being interpreted by criteria recommended by the U.S. Army and by the Centers for Disease Control. Specimens were classified as positive if bands were present at gp-41 or p-24 and p-55. Other banding patterns were considered to be negative.

In late 1987, the FDA licensed the first HIV western blot kit. For the first time, mandated criteria for interpretation of western blot banding patterns was available. Under the new criteria, a specimen was classified as positive if bands were present at p-24, p-31, and either gp-41 or gp-160/120. However, the only western blot results were classified as negative only if no bands were detected. Any western blot bands detected that did not meet the criteria for a positive result or a negative result were considered INDETERMINATE. The vast majority of these new indeterminate results would have been reported as negative by the previous interpretation criteria. In fact, under the new criteria, "indeterminate" results outnumbered positive results by approximately two-to-one. This caused a major dilemma for the insurance industry. Applicants with "indeterminate" western blot results were either declined or postponed pending further testing several months later.

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Pioneering work in the use of recombinant ELISA methods to resolve indeterminate western blot results was being done at the Walter Reed Army Institute of Research under the direction of Drs. Burke and Redfield.¹ Their research clearly demonstrated that individuals that were non-reactive by gp-41/gp-120 recombinant ELISA and indeterminate by western blot failed to seroconvert and were, indeed, HIV antibody negative. By the end of 1988 insurance laboratories were beginning

to use recombinant ELISA methods to resolve indeterminate western blot results.

Reference

1. Burke DS, Brandt BL, Redfield RR, Lee TH, et al. Diagnosis of human immunodeficiency virus infection by immunoassay using a molecularly cloned and expressed virus envelope polypeptide. Comparison to western blot on 2707 consecutive serum samples. *Ann Intern Med* 1987;106(5):671-676.
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