
BETA-2 MICROGLOBULIN AS A MARKER FOR HIV INFECTION

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Abstract

Beta-2 microglobulin is a sensitive surrogate test for HIV infection for use in jurisdictions where HIV antibody tests are not allowed to be performed on life insurance applicants by law/regulation.

The advantage of beta-2 microglobulin over T cell testing, which is a surrogate test also used by the life insurance industry for detecting HIV infection, is the stability of B₂M in serum over long periods of time.

The beta-2 microglobulin (B₂M) is a polypeptide (MW 11,4000) which constitutes the light chain of the HLA antigens. Although beta-2 microglobulin is present on all nucleated cells, it is produced predominantly by lymphocytes.¹ The turnover of the cell membrane is the main source of serum beta-2 microglobulin which is excreted by the kidneys. Normally, only trace amounts of beta-2 microglobulin are excreted in the urine. The serum concentration is increased when production is increased, which occurs mainly in some lymphoproliferative disorders, and seems to correlate with the size of the tumoral mass and/or with the turnover of the lymphocyte population, provided that renal function is normal. Abnormally elevated serum beta-2 microglobulin concentrations have been reported in renal failure, immunoreactive states (i.e., rheumatoid arthritis), Sjogren's Syndrome, malignant tumors, and in lymphoproliferative disorders. In renal disease, the serum level of B₂M reflects the glomerular filtration rate more accurately than serum creatinine. Normal serum levels

range from 0.9-2.4 mg/L; it has also been measured in plasma, urine, saliva, and cerebrospinal and pleural fluids.

Acquired immune deficiency syndrome (AIDS) is characterized by a defect in cellular immunity lymphopenia, and a depressed ratio of helper to suppressor T lymphocytes.² In 1982, Francioli, et al, first reported an elevation of B₂M levels in a homosexual man who presented with generalized lymphadenopathy (PGL) and later developed AIDS.³

Subsequently, Bhalla, et al, observed elevated B₂M levels in 29 of 31 patients with AIDS.⁴ These findings were confirmed and extended to include patients with PGL. Zolla-Pozner, et al, found that of 40 asymptomatic homosexual men followed prospectively, six of the seven with elevated B₂M eventually developed AIDS or ARC.⁵ All patients studied by Zolla-Pozner with confirmed or suspected AIDS were found to have elevated levels of serum B₂M.

Moss, et al, reported the three-year actual progression rate to the acquired immune deficiency syndrome (AIDS) was 22 percent in a cohort of men in San Francisco who were seropositive for HIV. An additional 26 (19 percent) developed AIDS-related conditions. B₂M concentration, packed cell volume, HIV p24 antigenaemia, and the proportion and number of T4 lymphocytes each independently predicted progression to AIDS. B₂M was the most powerful predictor.⁶ This paper, as well as four other presentations at the III International Conference of AIDS in 1987, demonstrated the prognostic value of B₂M in the clinical course of HIV infection.

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Conclusion

These studies demonstrate that beta-2 microglobulin is a sensitive surrogate test for predicting the extent and severity of HIV infection.

Seroconversion marks the beginning of the chronic stage in the natural progression of HIV infection. At this stage, there is a detectable surge in antibody production, a slowdown in detectable viral expression, increased T4 cell depletion, and increased levels of beta-2 microglobulin which herald the onset of symptoms and reflect the degree of immunodeficiency. The levels of beta-2 microglobulin continue to rise through the crisis stage of infection.

Since all life insurance applicant blood testing for underwriting purposes is collected in the field and forwarded to a laboratory for analysis, it is critical that an analyte can sustain the rigors of transportation, and does not degrade over time. Serum B₂M is stable in serum, and samples can be stored for long periods of time.

For the insurance industry it has a distinct advantage over T-Cell testing, because accurate measurement is

not dependent on immediate analysis (i.e., within 24 hours) by the laboratory. T-Cell testing does have a time requirement.

Beta-2 microglobulin can effectively be used in those jurisdictions where the HIV antibody tests have been disallowed by regulation.

References

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