

Role of Alcohol Abuse in Nutritional Immunosuppression^{1,2}

BERNHARD WATZL AND RONALD R. WATSON³

Alcohol Research Center Specialized, Department of Family and Community Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724

ABSTRACT Nutritional status is an important determinant of the host resistance against infections and tumors. Alcohol interferes in various ways with the complex system of nutritional immunomodulation. Alcohol acts directly on mechanical barriers in the gastrointestinal tract and increases permeability of intestinal walls, which results in a reduced exclusion of immunogenic material in the intestine. Alcohol further affects granulocytopenia and suppresses various immune functions. Indirect effects on the immune response are caused by alcohol-induced malnutrition. Heavy alcohol abuse is associated with a high energy intake derived by alcohol and an inadequate intake of protein, vitamins and minerals. In addition, alcohol abuse impairs absorption, utilization, storage and excretion of nutrients, which together with inadequate nutrient intakes results in nutritional immunosuppression. The high incidence of infections in alcoholics could be one consequence of the alcohol-induced immunosuppression. *J. Nutr.* 122: 733-737, 1992.

INDEXING KEY WORDS:

- alcohol abuse • nutritional status
- immunotoxic effects • host defense
- immunocompetence

Nutritional status is one major extrinsic factor determining the efficiency of the immune and host defense systems (1, 2). Chronic alcoholism is considered the most common cause of malnutrition in affluent societies of the western world (3), indicating a high risk of nutritional immunosuppression in chronic alcoholics. Alcohol can act at least at two different levels on the suppression of the immune response and non-specific host defense. As a nutrient, alcohol has a direct toxic effect on cells and organs of the host defense system. Alcohol further affects the nutrient intake and impairs absorption, utilization, storage and excretion of nutrients, and thereby may induce malnutrition, which affects immunocompetence. Alcohol-induced malnutrition together with the direct immunotoxic effects of alcohol may reduce the effectiveness of the host defense against infections. Epidemiological data

have shown that infectious and contagious illnesses are the most common cause of death in alcoholics (4, 5). Human immunodeficiency virus (HIV)-positive individuals who abuse alcohol could be exposed to a higher risk for opportunistic infections (6).

The per capita consumption of pure alcohol of the U.S. population aged 14 or older in 1987 was 21 g/d (7). Nine percent of all adults in the United States can be considered as heavy drinkers with ≥ 80 g of alcohol consumed per day (8). However, combined data from various surveys indicate that chronic alcoholics consumed an estimated mean of 193 g of alcohol/d or 43% of their energy intake was in the form of alcohol (9-13).

DIRECT EFFECTS OF ALCOHOL ON HOST DEFENSE

Interference of alcohol with mechanical host defenses and alteration of immune mechanisms are important factors that predispose alcohol abusers to an increased risk of infections. The main function of the gastrointestinal tract as a mechanical barrier in the host defense system is to control the intestinal flora and to prevent antigens from entering the system. Gastric acid secretion is an important regulator of the growth of the intestinal flora. Chronic alcoholics have a re-

¹ Presented as part of a symposium: Nutrition, Immunomodulation and AIDS, given at the 75th Annual Meeting of the Federation of American Societies for Experimental Biology, Atlanta, GA, April 25, 1991. The symposium was sponsored by the American Institute of Nutrition and supported in part by grants from Campbell Institute for Research and Technology, Clintec International Inc., Bristol-Myers Company and Mead Johnson Research Center. Guest editor for this symposium was R. R. Watson, Department of Family and Community Medicine, University of Arizona, Tucson, AZ.

² This research was supported by National Institutes of Health grant AA08037.

³ To whom correspondence should be addressed: Department of Family and Community Medicine, University of Arizona Health Sciences Center, 1501 North Campbell Avenue, Tucson, AZ 85724.

duced secretion of gastric acid, which could contribute to the increased incidence of jejunal bacterial overgrowth found in chronic alcoholics (14–16). An elevated intestinal permeability to a number of substances, including bacterial endotoxin, has been shown in chronic alcoholics (14–16). The increased inter- and intracellular permeability causes a high endotoxin exposure of cytokine-producing cells of the liver, which might result in the induction of enhanced monokine secretion. Elevated serum levels of interleukin-1, interleukin-6 and tumor necrosis factor are normally found in chronic alcoholics with liver disease (17). The deterioration of the intestinal mucosal barrier may promote absorption of immunogenic substances into the systemic circulation. At the same time, the clearance of antigens from circulation by Kupffer cells is impaired, which could explain in part the increased concentration of serum immunoglobulins found in alcoholics with alcoholic liver disease (18).

Chronic alcohol consumption appears to depress the production of polymorphonuclear leukocytes in the bone marrow. Up to 8% of alcoholics admitted to hospitals have granulocytopenia, which disappears after several days of abstinence. Bone marrow examinations showed a decreased number of mature granulocytes and a decreased reserve capacity for these cells in alcoholics (19). The absence of a bone marrow reserve and the inability to produce large numbers of new leukocytes expose alcoholics to increased risk when challenged by a severe bacterial infection. However, the release of leukocytes from the bone marrow is not inhibited by acute and chronic alcohol exposure of humans (19).

Animal studies demonstrated that chronic alcohol feeding induces atrophy of the thymus and spleen (20). There is evidence that the majority of the cells lost from the thymus after short-term alcohol ingestion are of an immature phenotype (CD4⁻/CD8⁻) (21). In rats, 13 mo of alcohol feeding reduced the total number of T lymphocytes from the spleen significantly. However, the percentage of lymphocytes with markers for T-helper cells was higher in spleens from alcohol-fed rats (22). So far, there are no data available about alcohol-induced thymus and spleen atrophy in humans. Long-term, high intakes of alcohol in animals and humans may alter the kinetics of production and turnover rates of lymphocytes in the thymus and spleen, with a resultant shift in relative concentration of lymphocyte subpopulations. Alcohol also exerts direct effects on immunocompetent cells. Because chronic alcoholics are often malnourished with liver disease and underlying infections, data from them about the immunotoxic effects of alcohol have to be analyzed very carefully. Acute and chronic alcohol ingestion prevent the normal delivery of neutrophilic granulocytes to sites of bacterial invasion and impair the ability of these cells to adhere to cell surfaces (18). Moreover, chronic alcohol abuse results in a decreased

chemotaxis of these cells, which contributes to the frequency and severity of infections in drinkers (18). The mononuclear phagocytizing system is another component of the immune system that is impaired by the toxic effects of alcohol. Phagocytosis, bactericidal activity and adhesion are reduced in these cells after *in vitro* exposure to alcohol (23). Alcohol further modulates the cytotoxic activity of natural killer cells. So far, the published data are very contradictory. Natural killer cells from nonalcoholic volunteers showed a decreased cytotoxicity in the presence of alcohol (24). However, alcoholics without liver disease demonstrated a normal natural killer cell activity (25, 26). Mice given alcohol for 1–4 wk showed a normal (27) and decreased (28, 29) natural killer cell activity. Antibody-dependent cellular cytotoxicity (30), lymphocyte proliferation response (31) and B lymphocyte function (32) are also impaired by alcohol. The first metabolite in the metabolism of alcohol, acetaldehyde, is further known to affect various immune functions (33, 34).

INDIRECT EFFECTS OF ALCOHOL ON IMMUNOCOMPETENCE: ALCOHOL-INDUCED MALNUTRITION

A variety of factors have an impact on the nutritional status of alcohol abusers, including the amount and duration of alcohol intake, the amount and quality of diets consumed, gastrointestinal and hepatic conditions, the socioeconomic status, diarrhea, vomiting as well as the loss of appetite in chronic alcoholics. High alcohol intake correlates with a high frequency of missed or partly eaten meals, which results in an inadequate and imbalanced intake of nutrients, probably the most important cause of alcoholic malnutrition. Combined data from various surveys about the macronutrient intake show that these alcohol abusers had a high intake of alcohol, which supplied nearly half of the total energy (9–13). Alcohol energy was added to the diet rather than replacing other food. The mean protein intake of the alcohol abuser exceeded 50 g/d, which would be adequate according to the RDA (35). However, it is possible that protein requirements are increased in alcoholics. It has been demonstrated that 62% of heavy alcohol abusers without liver disease and with RDA-adequate protein intake showed signs of protein malnutrition (13).

Even with an adequate intake of macronutrients, the addition of nonnutritive energy from alcohol may cause vitamin and mineral deficiencies. The incidence of vitamin and mineral deficiencies is correlated with the social status of the alcohol abuser. Alcoholics of a lower socioeconomic status have generally a higher chance to be malnourished (13–100%) than middle-class alcoholics (0–29%) (36). Besides the social class,

the amount and duration of alcohol consumption influences the micronutrient intakes in alcoholics.

Recent studies have shown that intakes of various micronutrients in chronic alcoholics are below the RDA. For example, up to 75% of alcoholics did not reach the recommendation for vitamin A (10, 12, 37, 38). Other vitamins with commonly insufficient intakes in alcoholics are vitamin C (75% of the alcoholics had an intake below the RDA) (10, 37, 39), thiamin (78%) (10, 12, 37, 38), folic acid (78%) (12) and niacin (66%) (10, 39). The recommendations of the National Research Council for nonalcoholic healthy individuals are used as the reference for the assessment of adequate or inadequate nutrient intakes in alcoholics. However, no information is available about the micronutrient requirements for individuals consuming up to 50% of their energy in form of alcohol, which are certainly higher than those for nonalcohol-consuming healthy individuals. If this is indeed the case, the frequency of inadequate micronutrient intakes in alcohol abusers would be higher as it is reported in various studies.

The nutrient intake alone, however, is not sufficient for the evaluation of the nutritional status of alcohol abusers. Biochemical and anthropometric measurements are needed additionally because alcohol has an impact on the absorption, utilization, storage and excretion of micronutrients. Alcohol has direct effects on the structure, function and motility of the small intestine (14, 16). These effects vary depending on the concentration of alcohol that is consumed. As a consequence, malabsorption of water-soluble vitamins is common to a moderate degree in alcohol abusers. Acute alcohol intake reduces the active absorption of folic acid. In chronic alcoholics, folic acid absorption was only impaired by alcohol in malnourished individuals (14). Acute alcohol further inhibits the uptake of thiamin and ascorbic acid, whereas chronic alcohol abuse decreases the absorption of thiamin and vitamin B-12 (16). There are no data published showing an impairment of the absorption of fat-soluble vitamins with alcohol abuse.

Alcohol interferes with the metabolism and utilization of various nutrients. For example, the conversion of thiamin to its active form as well as the utilization of the active form are affected by alcohol (40). Further, the hepatic formation and the release of 5-methyl-tetrahydrofolic acid, the conversion of pyridoxine to its active form and the hepatic activation of vitamin A are all impaired by alcohol (40). Alcoholics with fatty liver demonstrated decreased hepatic concentrations of water-soluble vitamins and of vitamin A (41). In alcoholics with alcoholic liver disease, hepatic vitamin A levels progressively decrease with increasing severity of liver injury (42). Alcohol induces hepatic microsomal enzymes for the oxidation of retinol to polar metabolites, which increases the hepatic vitamin A depletion (42). In addition, alcohol promotes vitamin A mobilization from the liver (43). Al-

coholic subjects without cirrhosis excrete abnormally large amounts of zinc in the urine (12). Increased urinary losses of calcium, magnesium and phosphate have also been reported after alcohol ingestion (41). The combination of reduced nutrient intake, decreased absorption, utilization and storage increased excretion, as well as the increased requirements, affect the antioxidant status in alcohol abusers. Several studies have shown that the serum antioxidant status (α -tocopherol, retinol, β -carotene, selenium, zinc) in alcoholics is significantly decreased compared with controls (44-46). All these antioxidants exert a strong impact on immunocompetence and the reduced serum concentrations of these micronutrients may contribute to the nutritional immunosuppression observed in heavy alcohol abusers. Clearly, the multiple effects of alcohol abuse on the nutritional status may result in malnutrition in these subjects with its known effect on immune functions (1, 2).

COMBINED EFFECT OF ALCOHOL AND MALNUTRITION ON IMMUNOCOMPETENCE

So far, very few studies have investigated the combined effects of heavy alcohol consumption and alcohol-induced malnutrition on the immunocompetence in alcohol abusers under controlled conditions. In one study with six noncirrhotic alcoholics who were fully restored in nutrition, subjects were supplied with 320 mL of pure alcohol/d for 20 d (47). Immunological tests were performed before and after that period. This study revealed remarkably little alteration of immune responses in well-nourished alcoholics given a large amount of alcohol. Chemotaxis was the only function found to be diminished with the high alcohol intake. The data from this and other similar studies (48) clearly demonstrate that alcohol-mediated immune cell damage only occurs in malnourished alcoholics.

The cytotoxic activity of natural killer cells from alcoholics with liver disease is reduced compared with healthy control subjects and with alcoholics without liver disease (25, 26). The poorer the nutritional status of the alcoholics with liver disease, the more severe was the deficit in natural killer cell activity. Response to standard skin testing in alcoholics without liver disease was also impaired (13). Twenty-nine percent of the alcoholics showed anergy to the skin testing, while 62% of them were malnourished, which again emphasizes the combined immunotoxic effects of malnutrition and alcohol. These few studies suggest that only the combination of heavy alcohol intake and malnutrition results in immunosuppression. However, more studies with alcohol abusers without liver disease are needed to study the immunosuppressive effects of alcohol.

DOES ALCOHOL ABUSE PREDISPOSE FOR HIV INFECTIONS?

Many clinical studies have reported increased susceptibility to infection in alcohol abusers and a lack of normal response to infections in alcohol-fed animals (5, 6). The direct immunotoxic effects of alcohol and the effect of alcohol-induced malnutrition on the immune status may predispose alcohol abusers to the reported higher risk of infections. Recently, several authors speculated on the role of alcohol as a cofactor in HIV infection and progression to acquired immunodeficiency syndrome (AIDS) (49, 50). Possible roles of alcohol abuse in enhancing HIV infection were by suppressing host defense and by facilitating viral entry through mucosal tissue. No evidence exists, so far, that alcohol abuse is directly associated with the development of AIDS. In a multicenter cohort study of homosexual men, the role of alcohol in accelerating immunodeficiency in HIV-positive individuals during an 18-mo period was studied (51). Alcohol drinkers showed no significantly higher risk of AIDS than nondrinkers. However, the group with the highest alcohol intake was defined by having two cans of beer or more per day. By mixing moderate with heavy alcohol drinkers the immunosuppressive effects of heavy alcohol abuse may have been diluted. This point really questions the significance of the study. Natural killer cells from AIDS patients exposed to alcohol in the test tube are depressed in their capacity to destroy tumor cells, which was not seen with natural killer cells from healthy individuals (52). HIV-positive individuals abusing alcohol could increase their risk of opportunistic infections and accelerate the progression of HIV infection to active AIDS by depressing the immune mechanisms that control the immunosuppressive impact of HIV (50).

In summary, alcohol is a nutrient that directly impairs host defense mechanisms and immune functions. Heavy alcohol abuse further induces malnutrition and in consequence immunosuppression. Chronic alcoholics are therefore exposed to a high risk of infections, including HIV. Immunosuppression, directly by alcohol and its metabolites and indirectly by malnutrition, has real potential to change resistance to HIV and to accelerate the progression of HIV infection to active AIDS.

LITERATURE CITED

1. Watson, R. R., ed. (1984) *Nutrition, Disease Resistance, and Immune Function*, Marcel Dekker, New York, NY.
2. Chandra, R. K., ed. (1988) *Nutrition and Immunology*, Alan R. Liss, New York, NY.
3. Thomson, A. D., Jeyasingham, M. D. & Pratt, O. S. (1987) Possible role of toxins in nutritional deficiency. *Am. J. Clin. Nutr.* 45: 1351-1360.
4. Cooper, B. & Maderazo, E. G. (1989) Alcohol abuse and impaired immunity. *Infect. Surg.* March: 94-101.
5. Adams, H. G. & Jordan, C. (1984) Infections in the alcoholic. *Med. Clin. North Am.* 68: 179-200.
6. Sternbach, G. L. (1990) Infections in alcoholic patients. *Emerg. Med. Clin. North Am.* 8: 793-803.
7. Seventh Special Report to the U.S. Congress on Alcohol and Health (1990) U.S. Department of Health and Human Services, Washington, DC.
8. Sixth Special Report to the U.S. Congress on Alcohol and Health (1987) U.S. Department of Health and Human Services, Washington, DC.
9. Patek, A. J., Toth, E. G., Saunders, M. G., Castro, A. M. & Engel, J. J. (1975) Alcohol and dietary factors in cirrhosis. *Arch. Intern. Med.* 135: 1053-1057.
10. Hurt, R. D., Higgins, J. A., Nelson, R. A., Morse, R. M. & Dickson, R. E. (1981) Nutritional status of a group of alcoholics before and after admission to an alcoholism treatment unit. *Am. J. Clin. Nutr.* 34: 386-392.
11. Simko, V., Connell, A. M. & Banks, B. (1982) Nutritional status in alcoholics with and without liver disease. *Am. J. Clin. Nutr.* 35: 197-203.
12. Mills, P. R., Shenkin, A., Anthony, R. S., McLelland, A. S., Main, A. N. H., MacSween, R. N. M. & Russell, R. I. (1983) Assessment of nutritional status and in vivo immune responses in alcoholic liver disease. *Am. J. Clin. Nutr.* 38: 849-859.
13. Mendenhall, C. L., Anderson, S., Weesner, R. E., Goldberg, S. J. & Crolic, K. A. (1984) Protein-calorie malnutrition associated with alcoholic hepatitis. *Am. J. Med.* 76: 211-222.
14. World, M. J., Ryle, P. R. & Thomson, A. D. (1985) Alcoholic malnutrition and the small intestine. *Alcohol Alcohol.* 20: 89-124.
15. Kozol, R. A. & Elgebaly, S. A. (1990) Ethanol and its effects on mucosal immunity. In: *Drugs of Abuse and Immune Function* (Watson, R. R., ed.) pp. 19-28, CRC Press, Boca Raton, FL.
16. Persson, J. (1991) Alcohol and the small intestine. *Scand. J. Gastroenterol.* 26: 3-15.
17. Watzl, B. & Watson, R. R. (1991) Alcohol and cytokine secretion. In: *Alcohol, Immunology and Cancer* (Yirmiya, R. & Taylor, A. N., eds.) CRC Press, Boca Raton, FL.
18. McGregor, R. R. (1986) Alcohol and immune defense. *J. Am. Med. Assoc.* 256: 1474-1479.
19. Liu, Y. K. (1980) Effects of alcohol on granulocytes and lymphocytes. *Semin. Hematol.* 17: 130-136.
20. Tennenbaum, J. I., Ruppert, R. D., St. Pierre, R. L. & Greenberger, N. (1969) The effect of chronic alcohol administration on the immune responsiveness of rats. *J. Allergy Clin. Immunol.* 44: 272-281.
21. Jerrells, T. R., Smith, W. & Eckardt, M. J. (1990) Murine model of ethanol-induced immunosuppression. *Alcoholism Clin. Exp. Res.* 14: 546-550.
22. Mufti, S. I., Prabhala, R., Moriguchi, S., Sipes, I. G. & Watson, R. R. (1988) Functional and numerical alterations induced by ethanol in the cellular immune system. *Immunopharmacology* 15: 85-94.
23. Rimland, D. (1983) Mechanisms of ethanol-induced defects of alveolar macrophage function. *Alcoholism* 8: 73-76.
24. Nair, M. P. N., Kronfol, Z. A. & Schwartz, S. A. (1990) Effects of alcohol and nicotine on cytotoxic functions of human lymphocytes. *Clin. Immunol. Immunopathol.* 54: 395-409.
25. Charpentier, B., Franco, D., Paci, L., Charra, M., Martin, B., Vuitton, D. & Fries, D. (1984) Deficient natural killer cell activity in alcoholic cirrhosis. *Clin. Exp. Immunol.* 58: 107-115.
26. Ledesma, F., Echevarria, S., Casafont, F., Lozano, J. L. & Pons-Romero, F. (1990) Natural killer cell activity in alcoholic cirrhosis: Influence of nutrition. *Eur. J. Clin. Nutr.* 44: 733-740.
27. Abdallah, R. M., Starkey, J. R. & Meadows, G. G. (1983) Alcohol and related dietary effects on mouse natural killer-cell activity. *Immunology* 50: 131-137.

28. Meadow, G. G., Blank, S. E. & Duncan, D. D. (1989) Influence of ethanol consumption on natural killer cell activity in mice. *Alcoholism Clin. Exp. Res.* 13: 476-479.
29. Blank, S. E., Duncan, D. A. & Meadows, G. G. (1991) Suppression of natural killer cell activity by ethanol consumption and food restriction. *Alcoholism Clin. Exp. Res.* 15: 16-22.
30. Walia, A. S., Pruitt, K. M., Rodgers, J. D. & Lamon, E. W. (1987) In vitro effect of ethanol on cell-mediated cytotoxicity by murine spleen cells. *Immunopharmacology* 13: 11-24.
31. Mutchnick, M. G. & Lee, H. H. (1988) Impaired lymphocyte proliferative response to mitogen in alcoholic patients. Absence of a relation to liver disease activity. *Alcoholism* 12: 155-158.
32. Aldo-Benson, M. (1990) Ethanol and the B-cell: Humoral immunity. In: *Drugs of Abuse and Immune Function* (Watson, R. R., ed.) pp. 175-183, CRC Press, Boca Raton, FL.
33. Levallois, C., Mani, J. C. & Balmes, J. L. (1987) Sensitivity of human lymphocytes to acetaldehyde: Comparison between alcoholic and control subjects. *Drug Alcohol Depend.* 20: 135-142.
34. Walia, A. S., Pruitt, K. M., Dillehay, D. L., Marshall, G. M. & Lamon, E. W. (1990) In vitro effect of acetaldehyde on cell-mediated cytotoxicity by murine spleen cells. *Alcoholism Clin. Exp. Res.* 13: 766-771.
35. Committee on Diet and Health, Food and Nutrition Board (1989) *Diet and Health* (National Research Council, ed.), National Academy Press, Washington, DC.
36. Derr, R. F., Porta, E. A., Larkin, E. C. & Rao, G. A. (1990) Is ethanol per se hepatotoxic. *J. Hepatol. (Amst.)* 10: 381-386.
37. Hillers, V. N. & Massey, L. K. (1985) Interrelationships of moderate and high alcohol consumption with diet and health status. *Am. J. Clin. Nutr.* 41: 356-362.
38. Rissanen, A., Sarlio-Lahteenkorva, S., Alfthan, G., Gref, C. G., Keso, L. & Salaspuro, M. (1987) Employed problem drinkers: A nutrition risk group? *Am. J. Clin. Nutr.* 45: 456-461.
39. Bunout, D., Gattas, V., Iturriaga, H., Perez, C., Pereda, T. & Ugarte, G. (1983) Nutritional status of alcoholic patients: Its possible relationship to alcoholic liver damage. *Am. J. Clin. Nutr.* 38: 469-473.
40. Darnton-Hill, J. (1989) Interactions of alcohol, malnutrition and ill health. *World Rev. Nutr. Diet.* 59: 95-125.
41. Morgan, M. Y. & Levine, J. A. (1988) Alcohol and nutrition. *Proc. Nutr. Soc.* 47: 85-98.
42. Leo, M. A. & Lieber, C. S. (1982) Hepatic vitamin A depletion in alcoholic liver injury in man. *N. Engl. J. Med.* 307: 597-601.
43. Leo, M. A. & Lieber, C. S. (1985) New pathway for retinol metabolism in liver microsomes. *J. Biol. Chem.* 260: 5228-5231.
44. Bjorneboe, G. E. A., Johnsen, J., Bjorneboe, A., Marklund, S. L., Skylv, N., Hoiseth, A., Bache-Wiig, J. E., Morland, J. & Drevon, C. A. (1988) Some aspects of antioxidant status in blood from alcoholics. *Alcoholism Clin. Exp. Res.* 12: 806-810.
45. Ward, R. J., Jutla, J. & Peters, T. J. (1988) Antioxidant status in alcoholic liver disease in man and experimental animals. *Biochem. Soc. Trans.* 17: 492.
46. Girre, C., Hispard, E., Therond, P., Guedj, S., Bourdon, R. & Dally, S. (1990) Effect of abstinence from alcohol on the depression of glutathione peroxidase activity and selenium and vitamin E levels in chronic alcoholic patients. *Alcoholism Clin. Exp. Res.* 14: 909-912.
47. Gluckman, S. J., Dvorak, V. C. & MacGregor, R. R. (1977) Host defenses during prolonged alcohol consumption in a controlled environment. *Arch. Intern. Med.* 137: 1539-1543.
48. Ericsson, C. D., Kohl, S., Pickering, L. K., Davis, J., Glass, G. S. & Faillace, L. A. (1980) Mechanisms of host defense in well nourished patients with chronic alcoholism. *Alcoholism Clin. Exp. Res.* 4: 261-265.
49. Molgaard, C. A., Nakamura, C., Hovell, M. & Elder, J. P. (1988) Assessing alcoholism as a risk factor for acquired immunodeficiency syndrome (AIDS). *Soc. Sci. & Med.* 27: 1147-1152.
50. Watson, R. R. (1990) Immunomodulation by alcohol: A cofactor in development of AIDS after retrovirus infection. In: *Cofactors in HIV-Infections and AIDS* (Watson, R. R., ed.) pp. 47-53, CRC Press, Boca Raton, FL.
51. Kaslow, R. A., Blackwelder, W. C., Ostrow, D. G., Yerg, D., Palenicek, J., Coulson, A. H. & Valdiserri, R. O. (1989) No evidence for a role of alcohol or other psychoactive drugs in accelerating immunodeficiency in HIV-1-positive individuals. *J. Am. Med. Assoc.* 261: 3424-3429.
52. Nair, M. P. N. (1991) Alcohol and AIDS. *Sci. Matters* 1: 27.