CHAPTER I

INTRODUCTION

Acquired Immune Deficiency Syndrome (AIDS) is a transmissible disease caused by a retrovirus called Human Immunodeficiency Virus (HIV)[1]. The virus infects T helper cells via the CD_4 receptors but can also infect other cell types via other mechanisms of entry[2,3,4,5,6]. The final outcome of the infection is the gradual destruction of CD_4^+ helper T cells which are the cells of central importance in the immune response[1,7,8]. The state of immunodeficiency so induced will render the patient susceptible to various opportunistic infections and malignancies, a state called full-blown AIDS.

Inspite of its first description in 1981 in USA, AIDS officially arrived in Thailand in late 1984. Many more AIDS cases and HIV infections were subsequently discovered particularly after the availability of anti-HIV testing in 1985[9]. The number of HIV-infected cases in Thailand increased sharply in 1988 due to the rapid increase of HIV infection among intravenous drug users (IVDU). The same trend of progressive increase of HIV infection has continued since 1988 (Table I). By the end of 1990, 25,342 Thais have been infected by HIV (76 with AIDS, 235 with AIDS related complex and 25,031 with asymptomatic HIV infections)[10].

Since HIV infection is relatively new in Thailand, its clinical manifestations and clinical course in Thai patients are largely unknown. It is possible that some of the clinical manifestations of the Thai patients may be different from those

in the developed world because of the difference in the indigenous environmental pathogens and the difference in nutritional status. Therefore, treatment and prognosis of HIV infection in Thai patients may be different from those of the other countries.

Table I: Yearly Incidence of AIDS, ARC and Asymptomatic HIV Infection in Thailand from 1984 to December 31, 1990

	1984	1985	1986	1987	1988	1989	1990	Total
AIDS	1	1	0	7	5	29	33	76
ARC	0	5	8	13	22	90	97	235
Asymptomatic	0	5	10	171	5,047	10,651	9,147	25,031
Total	1	11	18	191	5,074	10,770	9,277	25,342

Zidovudine (azidothymidine) is the only licensed anti-HIV drug available for human use[11]. However, not all symptomatic HIV patients can afford the drug due to its high cost. At the same time, ideally the drug should be started at a critical time period, i.e., at the beginning of immunologic and clinical deterioration in order to avoid toxicity and drug resistance [12,13]. Therefore, clinical and immunologic markers which can reliably predict the progression of HIV infection are of great importance to aid clinicians in initiating this expensive and potentially toxic drug.

Clinical and immunologic prognostic markers have been well studied in the Western hemisphere. The important clinical prognostic markers are oral candidiasis, oral hairy leukoplakia,

severe seborrheic dermatitis, pruritic impetigo, herpes zoster, chronic progressive and disseminated herpes simplex, prolonged fever, chronic diarrhea and unexplained weight loss[14,15,16].

The important immunologic prognostic markers include

-decreasing CD_4^+ T cells[17,18]

-increasing β_2-microglobulin level[19,20]

-increasing neopterin level[21,22,23,24]

-decreasing anti-p24 titer simultaneously with increasing p24 antigen level[25,26,27,28]

β_2-microglobulin and neopterin represent the activation of cell-mediated immune response. There are evidences that the activation of cell-mediated immunity can simultaneously increase HIV multiplication as well[21,24,29]. The decreasing CD_4^+ T cells indicates the destruction of CD_4^+ T cells by the virus.

These prognostic markers are useful for predicting disease progression. AIDS patients possess the highest levels of β_2-microglobulin and neopterin. These levels are successively lower in ARC , PGL and asymptomatic HIV respectively[19,22,23]. For CD_4^+ T cells , AIDS patients have the lowest number of CD_4^+ T cells, followed successively by patients with ARC and PGL and nearly normal in asymptomatic HIV[30,31]. HIV antigen (or p24 antigen) is usually undetectable. It has been demonstrated that the developmnt of AIDS is usually preceded by a decline in anti-p24 titer with HIV antigenemia[32,33]. However, all of these immunologic prognostic markers have not yet been well studied in Thai HIV patients.

Since Thai HIV-infected patients rapidly increase from the last two years, the prospective long-term study for appropriate laboratory prognostic markers which represents good correlation with disease progression will be useful for following

up these patients. In addition, these prognostic markers are also useful to be used for studying the effect of therapeutic drugs in these patients as well.

It is therefore the objective of this study to examine the reliability and the usefulness of some immunologic parameters in the follow-up of Thai HIV patients. The information obtained may also be used in future therapeutic or vaccine studies.