Age-related Changes in Subpopulations of Peripheral Blood Lymphocytes in Healthy Japanese Population

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Abstract: Peripheral blood mononuclear cells were obtained from healthy Japanese individuals ranging in age from 20 to 90 years old and analyzed by using three color flow cytometer with regards to the number and percentage of various lymphocytes. In addition, we assessed the proliferative capacity of T-cells in the presence of an anti-CD3 monoclonal antibody and the amount of cytokines produced in the supernatant.

The results showed that an age-related decline was observed in the numbers of CD3+ T-cells, CD8+ T-cells, naive T-cells, CD8+CD28+ T-cells, and B-cells and in the proliferative capacity of T-cells. The rate of decline in these immunological parameters except for the number of CD8+ T-cells was steeper in males than in females ($p<0.05$). An age-related increase was observed in the number of CD4+ T-cells, memory T-cells, and NK-cells and in the CD4/CD8 ratio. The rate of increase of these immunological parameters was steeper in females than in males ($p<0.05$). The T-cell proliferation index (TCPI), which was calculated based on T-cell proliferative activity and the number of T-cells, showed an age-related decline. The rate of decline in the TCPI was again steeper in males than in females ($p<0.05$). The score of immunological vigor calculated using 5 T-cells parameters also declined with age, and the rate of decline was steeper in males than in females ($p<0.05$). The
present study has confirmed the age-related changes in immunological parameters reported in literature. In addition, we found that a statistically significant difference was observed between males and females in some immunological parameters such as the number of T-cells and TCPI. The slower rate of decline in the immunological parameters studied in females than in males may be consistent with the fact that women survive for longer period of time than men.

1 Introduction

Immunological functions are known to decline with age in many animal models and humans (Linton and Dorshkind 2004; Utsuyama et al. 1992; Hirokawa et al. 2006). Understanding the level of immunological functions at an individual level is clinically important, since the immunological decline is accompanied by various diseases such as infections, cancer and vascular diseases.

Accumulating evidences mainly obtained from animal models have shown that age-related immunological decline mainly occurs in T-cell dependent immune functions, and is mainly caused by thymic involution that begins in the early phase of life (Hirokawa et al. 2006).

In humans, data regarding immunological functions are mainly obtained from blood serum and blood cells. Serum contains immunoglobulins, complements and cytokines. The levels of IgG and IgA in serum show a trend of increase with age (Suzuki et al. 1984). The level of complements does not change remarkably with age. The level of cytokines in healthy people is generally low. In contrast, the level of white blood cells (WBC) changes remarkably during disease and also with aging. WBC comprises granulocytes, lymphocytes and monocytes. There are various subpopulations of lymphocytes with different functions. Data regarding the age-related changes in lymphocytes and their functions are not sufficiently available as yet.

The purpose of this study is to provide immunological data on peripheral blood lymphocytes obtained from 162 male and 194 female healthy volunteers, ranging in age from 20 to 90 years. Our study discusses the age-related changes in subpopulations of peripheral blood lymphocytes from both immunological and gerontological viewpoints.

2 Materials and Methods

Blood specimens: Two milliliters of blood was taken in a tube containing ethylenediaminetetraacetic acid (EDTA-2K) for hematological analysis performed using a PENTRA80 analyzer (Horiba, Kyoto, Japan). Eight milliliters of blood was taken in a cell preparation tube (vacutainer, 362761, Becton Dickinson (BD), NJ) for collecting mononuclear cells and was used for immunological analyses.

Subjects: Healthy volunteers were selected based on clinical records and laboratory examinations. None of the blood donors were suffering from neoplastic or autoimmune disease; further, none were receiving any medications that could