MEDICAL SCIENCE MONITOR BASIC RESEARCH

MOLECULAR BIOLOGY

eISSN 2325-4416
© Med Sci Monit Basic Res, 2014; 20: 93-96
DOI: 10.12659/MSMBR.891239

Received: 2014.06.21
Accepted: 2014.06.23
Published: 2014.07.12

The effects of aging on lymphocyte subgroups in males and females

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Self financing

Background: Age-associated immune senescence is a catch-all phrase that has been used to describe a plethora of changes to the immune system across the lifespan. Aging is associated with a decline in immune function. Our aim in this study was to investigate how lymphocyte subgroups in peripheral blood are affected by aging among males and females.

Material/Methods: Study participants were 70 healthy individuals from 3 different age groups, observed from January 2010 to January 2012. The average levels of CD3+, CD4+, CD8+, CD19+, CD16+/CD56+, CD3+/CD69+, and CD19+/CD69+ were determined for each group and compared in terms of age and sex.

Results: We found significant reduction in the level of CD3+T cells related with age, but no significant changes in CD19+ B cell levels ($p<0.005$). Aging significantly reduces activated B cell (CD19+/CD69+) levels in males ($p<0.005$).

Conclusions: Our results show that there may be differences between males and females in terms of immune senescence.

MeSH Keywords: Aging • Lymphocytes • Lymphocyte Subsets

Full-text PDF: http://www.basic.medscimonit.com/abstract/index/idArt/891239

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

The world population is rapidly aging due to development of health care. At present, individuals can live for 80–100 years, much longer than in past generations. According to the WHO, the proportion of people over 60 years of age is increasing quickly and is expected to exceed 2 billion people worldwide by the year 2050 [1]. Immune senescence comprises a set of changes occurring to the innate and adaptive immune responses that accompany human aging [2]. Age-associated immune senescence is a catch-all phrase that has been used to describe a plethora of changes to the immune system over the lifespan. Aging is associated with a decline in immune function [3].

Immune aging is a complex process that comprises many reconstructions and regular changes rather than being a simple one-way reduction in all immune functions; thus, all parts of the immune system in immune senescence are not affected equally. For instance, it has been observed that natural immunologic structures that are common to all living things are less affected than are acquired immune system structures. Active participation of inflammation, which forms the most basic defense mechanism in the aging process, is also an indicator of this. The decline in immune function with age is unanimously recognized and supported by epidemiologic and clinical studies [4–6].

Many studies have demonstrated that immune functions and cells in the immune system are affected by aging. Some studies reported that differences in immune system due to aging vary between males and females. Sex-related differences in immune system susceptibility have also been observed in several mouse models and may be related to differences in the expression patterns of immune response genes [7]. Understanding the basis of sex and age differences in immune response genes is important for developing new approaches to prevention, diagnosis, and treatment of diseases. Our aim in this study was to investigate how lymphocyte subgroups in peripheral blood are affected by aging among males and females.

Material and Methods

Study participants were 70 healthy individuals from 3 different age groups, observed from January 2010 to January 2012. All patients were analyzed at the Baskent University Faculty of Medicine Immunology Department. Participants were divided into 3 different groups according age: Group 1 (n=20) was 25–45 years old (10 males, 10 females), Group 2 (n=25) was 45–65 years old (12 males, 13 females), and Group 3 (n=25) was older than 65 years old (13 males, 12 females). Venous blood samples were analyzed by lymphocyte immune phenotyping using flow cytometry. We determined the average levels of CD3+, CD4+, CD8+, CD19+, CD16+/CD56+, CD3+/CD69+, and CD19+/CD69+ by age group and sex. Individuals who were smokers or who had a chronic disease were excluded from the study. Collected data were statistically analyzed by Kruskal-Wallis-ANOVA, with $p<0.05$ considered to be statistically significant.

Results

Distribution of lymphocyte subgroups differed by sex and age groups (Table 1). We found a significant reduction in the rate of CD3+T cells related with age, but no significant change in CD19+ B cell rates ($p<0.005$). Another noteworthy result was that the level of CD8+T cells was lower in males compared to females and varied by age group ($p<0.005$). Level of activated T and B cells did not differ by age group, but levels of activated B cells (CD19+/CD69+) decreased with age in males ($p<0.005$) (Figure 1).

Table 1. Comparison of lymphocyte subgroups by age interval in males and females.

Age Interval	24–45		45–65		>65	
Total Lymphocytes%	Male	Female	Male	Female	Male	Female
CD3+	71.2±1.2	68.6±1.2	64.2±0.9	63.6±0.8	59.8±1.3	58.8±1.4
CD3+/CD4+	42.4±0.9	40.7±1.2	41.4±1.1	39.8±0.7	38.9±1.1	37.2±0.9
CD3+/CD8+	27.9±0.5	26.9±0.8	22.7±0.8	25.7±0.8	20.3±1.2	24.6±0.7
CD19+	11.2±0.3	10.8±0.2	10.6±0.4	9.9±0.1	9.8±0.2	9.7±0.2
CD16+/CD56+	17.3±0.4	17.8±0.3	22.4±0.5	18.6±0.2	29.4±0.4	20.2±0.3
CD3+/CD69+	1.83±0.06	1.76±0.05	1.74±0.08	1.69±0.07	1.72±0.03	1.65±0.04
CD19+/CD69+	0.20±0.01	0.18±0.01	0.13±0.02	0.17±0.01	0.07±0.09	0.16±0.01

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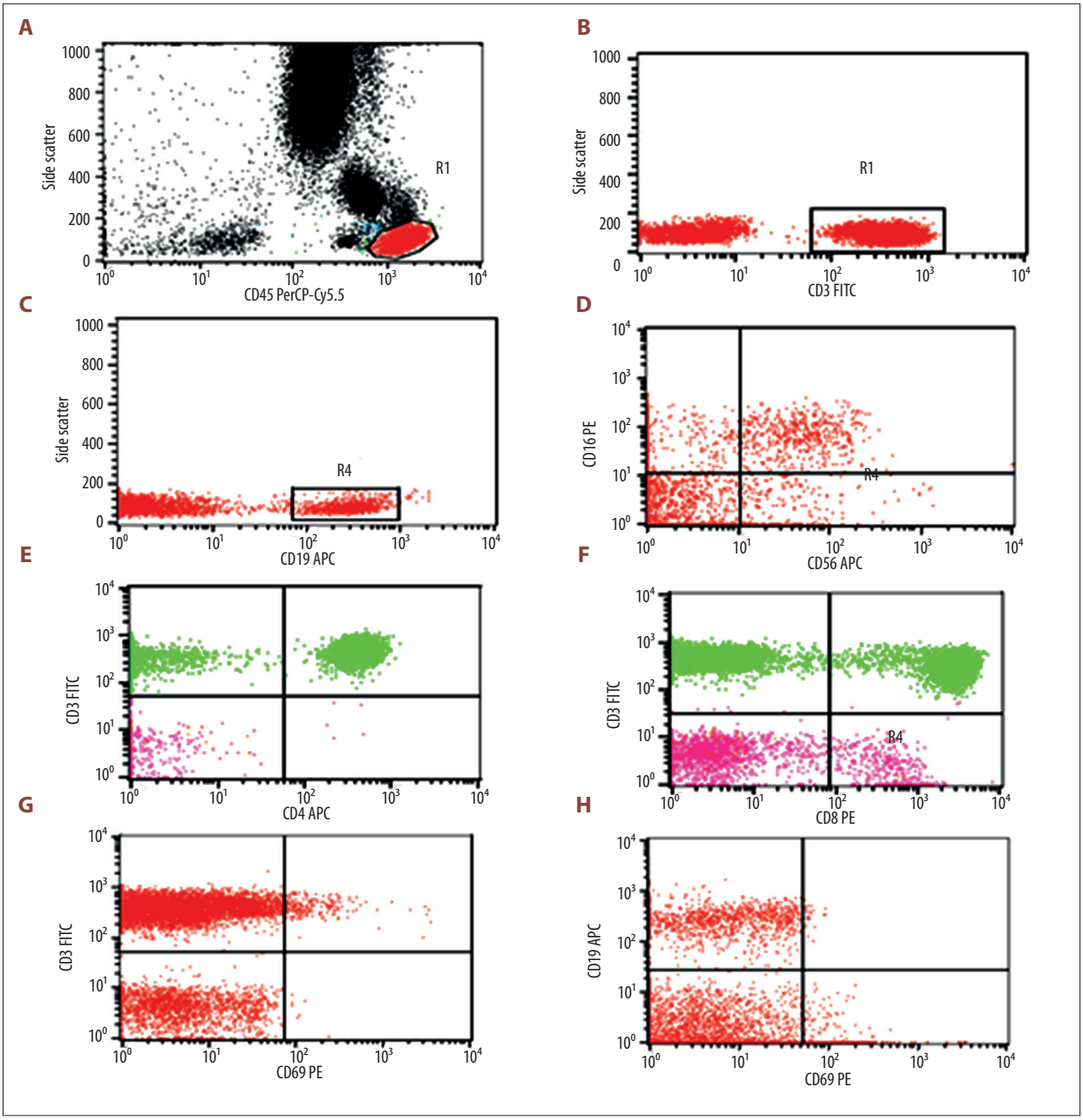

Figure 1. Analysis of lymphocyte subgroups with flow cytometry technique. (**A**) General view and lymphocyte selection. (**B**) CD3+ door. (**C**) CD19+ door. (**D**) CD16+/CD56+ togetherness. (**E**) CD3+/ CD4+ togetherness. (**F**) CD3+/CD8+ togetherness. (**G**) CD3+/ CD69+ togetherness. (**H**) CD19+ /CD69+ togetherness.

Discussion

Projections indicate that by 2025 the world population over age 65 will be increasing 3.5 times as rapidly as the total population and the proportion of individuals age 60 years and older, which accounted for 10% of the world population in 2000, will increase to approximately 22% of the world population by 2050 [8]. Aging is a highly complex and continuous process that affects almost all organ systems, causing molecular and physiological changes, both qualitatively and quantitatively. The aging of the immune system is a dynamic process that may at least partly reflect adaptation of the response to the evolving pathogen surroundings [1–6]. Aging is increasingly recognized as being associated with a pro-inflammatory state that plays an important role in the development of chronic diseases [9]. Immune senescence comprises a set of changes occurring to the innate and adaptive immune responses that accompany human aging. These result

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in complex manifestations of still poorly defined deficiencies in the elderly population [2,10].

In the evaluation of T and B cell activations, no change due to aging was observed in level of activated T cells. On the other hand, aging significantly reduces activated B cells level of males. Our results show that levels of activated T and B cells did not differ by age group. We found that that aging reduces activated B cell (CD19+/CD69+) levels of males. Males have shorter life expectancy than females due to the effects of aging making them more sensitive. The immune system in males differs from that in females [11]. In our study, we observed the lower CD8+T cell rates of males compared to those of females, especially when compared by age. However, these differences are thought to be very small. Therefore, we especially wanted to observe the changes in peripheral blood lymphocytes of males and females who belong to different age groups.

Recent studies have revealed that changes in the number of lymphocytes and a decrease in cell activation and proliferation appear with aging. However, the difference between males and females in immune senescence is still a hotly debated topic because many different factors may be involved. Differences between males and females in susceptibility to infection and differences in prevalence of autoimmune diseases by sex may help understand these differences in aging and health [2–5,12].

In general, it has been demonstrated in human and mouse studies that females produce stronger humoral and cellular immune responses against varied antigens than males do. This difference also plays a role in female allograph rejection, which has been demonstrated in mouse studies. Moreover, it is reported that effects of hormones may contribute to these differences. For instance, it is reported that female estrogen stimulation, which leads telomerase induction by c-myc, has an “anti-aging” effect. Another theory that has been put forward about this topic in recent years suggests that depending on the development needs mitochondria in female cells have a better adaptation than male cells have [11–13].

Conclusions

The immune response to infections, immunizations, and tumors in the elderly is quite different from that in young people. Our study shows that there may be differences between males and females in terms of immune senescence. Further research on this subject is needed.

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