

The Influence of Race on T-Cell Subset Distributions

David J. Tollerud¹, Linda Morris Brown, William A. Blattner, and Robert N. Hoover

Epidemiology and Biometry Program, National Cancer Institute, Bethesda, MD.

SUMMARY

To investigate the influence of race on the cellular immune system, we analyzed peripheral blood mononuclear cell subsets in 266 healthy nonsmoking adults and 112 healthy children. Among adults, blacks had a significantly higher proportion of B cells, a lower proportion of T cells, and a higher proportion of HLA-DR positive cells and activated T cells than whites. Among children, the proportion of HLA-DR positive cells and activated T cells were significantly higher in blacks than in whites, but the proportion of T cells and B cells were similar in blacks and whites. An apparent decrease in the proportion of CD4+ (T-Helper) cells was observed in black women age 50 and older compared to white women and younger black women. These and other race-related immunologic alterations may provide clues to the etiology of diseases and conditions which exhibit significant racial differences.

INTRODUCTION

Recent investigations have demonstrated that the immune system is quantitatively and qualitatively affected by numerous host factors, medical conditions and environmental exposures. Age, gender, allergies and exposure to cigarette smoke, for example, have all been associated with distinct alterations in T-cell subset distributions. Much less is known about the influence of race or ethnic background on the immune system. Blacks are known to have a lower leukocyte count due a relative decrease in neutrophils compared to whites (Karayalcian, Rosner and Sawitsky 1972; Van Assendelft 1985). Blacks are also reported to have a higher average IgE level than whites (Grundbacher 1975). Prince and colleagues reported significant race-related differences in T-cell subsets and natural killer cells between Asians and whites but found no significant differences for the limited number of blacks in the study (Prince, Hirji, Waldbeser et al. 1985). To address potential black:white differences in the cellular immune system, we analyzed peripheral blood mononuclear cell subsets in a population-based sample of healthy adults and their children (Tollerud, Clark, Brown et al. 1989; Tollerud, Ildstad, Brown 1990).

¹ Current Address: University of Pittsburgh Graduate School of Public Health Room A-718, Pittsburgh, PA 15261

METHODS

The study population was selected by random digit dialing from households in the Washington, D.C. metropolitan area. After screening to determine demographic characteristics and cigarette smoking status, a detailed questionnaire was administered to exclude individuals with illnesses, exposures or medical conditions which might affect the immunological parameters under investigation. The analyses presented here were limited to black and white nonsmoking adults and a sample of children ages 12-19 from the study households.

The following directly fluorescein conjugated monoclonal antibodies, purchased from Ortho Diagnostics, Raritan, NJ (ORTHO) or Becton Dickinson Monoclonal Center, Mountain View, CA (BD) were used in the analyses: OKT3 (CD3+ T-cells; ORTHO); OKT4 and OKT4A (CD4+ helper-inducer T-cell subset; ORTHO); OKT8 (CD8+ suppressor-cytotoxic T-cell subset; ORTHO); anti-Leu 12 (CD19+ B-cells; BD); anti-Leu M3 (CD14+ monocytes; BD); anti-Leu 11A (CD16+ natural killer cells; BD); anti HLA-DR (nonpolymorphic HLA-DR antigen; BD); and mouse IgG1 (clone 11-63; BD) and IgG(a+b) (clones 11-4.1 and MPC-11; BD) as negative control reagents. Single parameter flow cytometry analyses were performed on a FACS II cell sorter (BD, Mountain View, CA) using forward and right-angle light scatter gating. The relative proportion of activated T-cells (ACT-T) was estimated by subtracting from the HLA-DR+ cell pool the number of B-cells and the number of monocytes not eliminated by right-angle-scatter gating. Linear regression analysis was employed to evaluate the relative contributions of age, race, gender, and other independent variables on mononuclear cell subset proportions.

RESULTS AND DISCUSSION

The black:white differences we observed are summarized in Table 1. Among adults, blacks had a higher proportion of B cells, a lower proportion of T cells, and a higher proportion of HLA-DR+ cells than whites. The estimated proportion of activated T cells was also significantly higher in blacks than in whites and increased significantly with age (Fig. 1). Among the children, the increase in CD3+ cells among whites was not statistically significant, and there was no significant difference in CD19+ cells (Table 1). Like adults, black children had significantly higher levels of HLA-DR+ cells and activated T cells. Further analysis of gender and age strata also revealed that black women age 50 or older had a significantly lower proportion of CD4+ (T-Helper) cells compared to white women and younger black women ($p < 0.05$) (Fig. 2). No such discontinuity was observed for men. No significant differences in CD8+ (T-Suppressor/Cytotoxic) cells, CD16+ (Natural Killer) cells or CD14+ cells (monocytes) between blacks and whites.

One additional black:white difference confirmed in these studies was the previously reported heterogeneity of the T4 epitope of the CD4 cell surface antigen among blacks (Fuller, Trevithick, Fuller et al. 1984) (Fig. 3). The inheritance pattern has been shown to be a Mendelian co-dominant pattern, with a similar distribution of phenotypes among black populations world-wide. Affected individuals have normal numbers of CD4+ cells, and no functional differences associated with the T4 epitope heterogeneity have been reported.

Table 1. Black:Wh.

Cell Surface Anti	
ADULTS	
CD3	(T cells)
CD19	(B cells)
HLA-DR	"ACT-T" ³
CHILDREN	
CD3	(T cells)
CD19	(B cells)
HLA-DR	"ACT-T" ³

¹Values expressed
²p value from mult
influence of age
³ACT-T is a deriv
activated T-cells

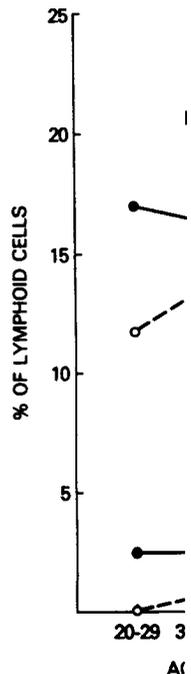


Figure 1: Influen cells (circles whites.

Table 1. Black:White Differences in Mononuclear Cell Subsets¹

Cell Surface Antigen	Whites	Blacks	p Value ²
ADULTS			
CD3 (T cells)	76.1 ± 0.05	73.6 ± 0.8	< 0.01
CD19 (B cells)	10.0 ± 0.3	11.8 ± 0.4	< 0.001
HLA-DR	14.0 ± 0.4	17.9 ± 0.6	≤ 0.0001
"ACT-T" ³	2.1 ± 0.4	4.0 ± 0.6	≤ 0.0001
CHILDREN			
CD3 (T cells)	74.7 ± 0.7	72.1 ± 1.5	NS
CD19 (B cells)	10.1 ± 0.6	9.4 ± 1.0	NS
HLA-DR	14.8 ± 0.5	17.1 ± 1.1	< 0.05
"ACT-T" ³	2.8 ± 0.6	6.0 ± 1.0	≤ 0.01

¹Values expressed as mean ± SE percentage of lymphoid cells

²p value from multiple linear regression model adjusting for the influence of age and gender. NS: p > 0.05

³ACT-T is a derived estimate of the proportion of circulating activated T-cells

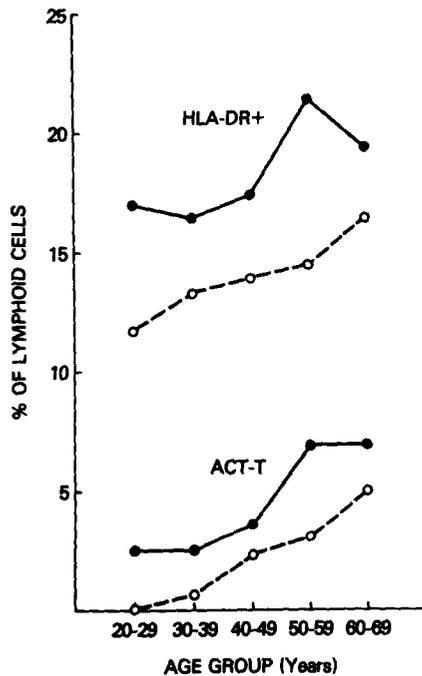


Figure 1: Influence of race and age on HLA-DR+ cells and activated T cells (ACT-T). Solid circles = black subjects; open circles = white subjects. p ≤ 0.0001 for blacks versus whites. (From Tollerud, Clark, Brown et al. 1989)

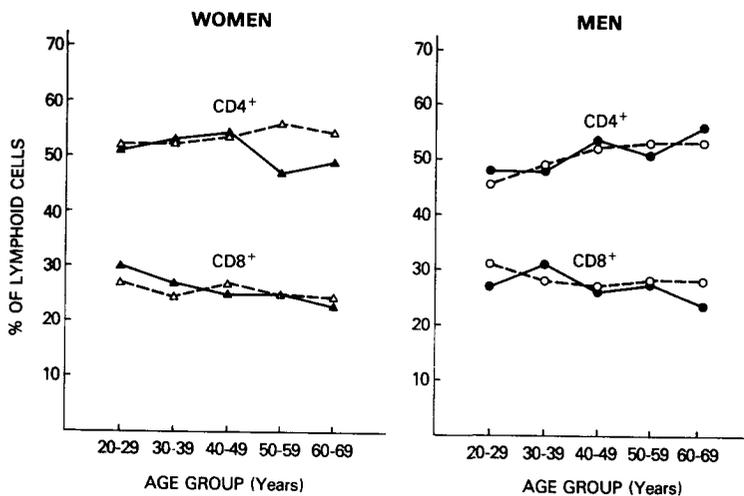


Figure 2: Influence of race and age on T-cell subsets in men and women. Solid triangles = black women; open triangles = white women; solid circles = black men; open circles = white men. (Adapted from Tollerud, Clark, Brown et al. 1989)

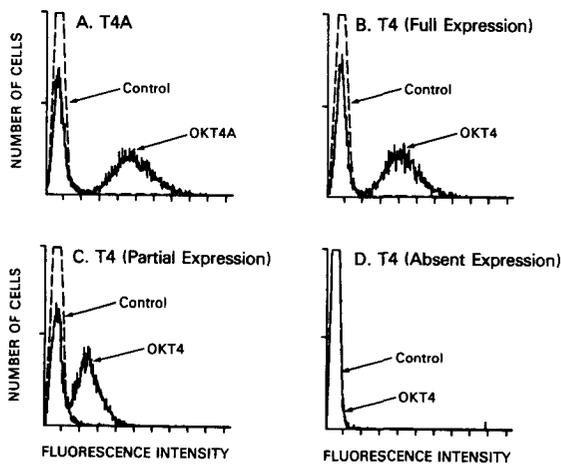


Figure 3: Differential expression of the T4 epitope in blacks and whites. A. Typical fluorescence intensity histogram for cells labeled with OKT4A; B. Full expression of the T4 epitope (100% of whites, 50-70% of blacks); Partial Expression (22-39% of blacks); and Absent Expression (4-11% of blacks). (From Tollerud et al. 1989 and 1990)

The clinical significance is uncertain. To date immunologic responses in blacks compared to whites and whites for a variety of diseases do not permit a clear picture of effects underlying racial differences directed at determining the role in those racial differences.

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The clinical significance of these race-related differences remains uncertain. To date, no significant functional differences in immunologic responses have been reported for different racial groups. Even the dramatically lower neutrophil count among blacks compared to whites has no known clinical correlates. However, these data emphasize that there are clear-cut differences between blacks and whites for a variety of immunologic parameters. Present data do not permit a clear distinction between genetic and environmental effects underlying these differences. Future efforts should be directed at determining whether such immunologic differences may play a role in those diseases and conditions which show distinct racial differences in incidence or severity.

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