ALTERATIONS OF HUMAN IMMUNE SYSTEM FUNCTIONS IN RELATION TO ENVIRONMENTAL CONTAMINATION, GENDER AND ALCOHOL CONSUMPTION INTENSITY

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SUMMARY

Environmental contamination and use of alcohol may be a cause of immune system disturbances and various diseases.

The aim of this study was to evaluate changes of different alcohol consumption intensity on the immune condition of women and men living in a district contaminated with industrial siftings (Trakai) and in a relatively clean district (Širvintos).

The immune system parameters were investigated in 282 Trakai district inhabitants (127 males and 155 females) and in 282 Širvintos district inhabitants (129 males and 153 females). Due to gender and alcohol consumption intensity the immune system functions were evaluated in the following groups: abstainers, light alcohol users, moderate alcohol users and alcohol abusers.

Absolute number of $CD5^+$, $CD4^+$, concentration of IgA in blood serum and some other investigated indices of light alcohol users were significantly increased in the male group of Trakai district in comparison with females of this district. However, in the same group of light alcohol drinkers of Širvintos district, males had lower indices ($CD5^+$, $CD4^+$, $CD4^+/CD8^+$, IgM) than females. Immune system parameters of males who were light and moderate alcohol users in Trakai district were stimulated in comparison with the same alcohol consumption groups of males in Širvintos district.

Our investigations showed that combination of environmental pollution and different intensity of alcohol consumption cause various alterations of immune system functions in males and females.

Key words: environmental contamination, intensity of alcohol consumption, gender, immunity

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INTRODUCTION

Immune system is very sensitive to effects of diverse toxic chemicals including environmental pollutants. Pollutants interact with immune system and can cause local or systemic alterations ranging from hyperactive immune responses to immunosuppression. Such alterations can modify the host defence mechanisms against many diseases, cancer among them (1, 2, 3).

Other lifestyle factors, as the use of alcohol, can also have an impact on human immune condition. Researches have shown association between drinking type of alcohol, its intensity and immune system functions (4, 5).

It is established that the effects of alcohol on the immune response are expressed differently in males and females (6). The same quantity of alcohol consumed for the same time period produces higher blood alcohol level in women than in men (7).

Our previous investigations showed that the immune condition of alcohol users depended on the place of residence and gender (8). Therefore we suppose that it is meaningful to study whether alcohol consumption intensity may cause different immunomodulation in female and male groups. Thus, the objective of this study was to distinguish the influence of different intensity of alcohol consumption on the immune condition of women and men living in a district contaminated with industrial siftings (Trakai) and in a relatively clean district (Širvintos).

This work is in continuation of publications of the state scientific program "Ecological Sustainability of Regional Development in a Historical Perspective: Lithuanian Case Studies (1992–1997)". The data already published dealt with the dependence of human immunity on environmental pollution, age and gender, with the changes of immune state with respect to tobacco smoking, alcohol consumption and cancer risk (8, 9, 10).

MATERIALS AND METHODS

Immunological investigations were carried out in Trakai (a contaminated district, with 60-62 t/km^2 of pollutants per year) and in Širvintos (a district slightly contaminated with $<1t/km^2$ of pollutants per year) (11).

The immune status was investigated in 282 persons (127 males and 155 females) who lived in a contaminated district (Trakai) and in 282 persons (129 males and 153 females) who lived for many years in a conventionally clearer district (Širvintos). The age of

the individuals studied was 20–64 years. In Trakai district 96% of persons used alcohol (99% of males and 93% of females), in Širvintos – 89% (96% of males and 82% of females). With respect to the strength of alcohol and the frequency of alcohol consumption the immunohaematological indices were investigated in the following four groups:

1. abstainers,
2. light alcohol users (people rarely using wine or bear),
3. moderate alcohol users (no less than 250 g of spirits 1–3 times per month),
4. alcohol abusers (more than 250 g of spirits once or more times per week).

The indices of cellular immunity determined for all the investigated persons by indirect immunofluorescence method using monoclonal antibodies (Sorbent, Russia) were the following: percentage and absolute number of T lymphocyte population ($CD5^+$), T helpers ($CD4^+$), T cytotoxic/suppressors ($CD8^+$), ($CD4^+/CD8^+$) ratio, B lymphocyte ($CD72^+$), NK cells ($CD16^+$). In addition, to evaluate the immune status, blasttransformation reaction, as well as 2 indices of blood neutrophils phagocytosis reaction (phagocytosis index – PhI and phagocytosis number – PhN) were employed. To evaluate the immunity humoral chain, concentration of IgG, IgA and IgM (N. F. Gamaleja Institute of Epidemiology and Microbiology of Academy of Medical Sciences, Russia) in blood serum was studied (12). The leukocyte formula was determined too.

The data were evaluated employing Student's test in accordance with the STATGRAPH program, and EXCEL program (version 5) in accordance with Confidence Interval Analysis method. The differences of comparative quantities were estimated as reliable at $p \leq 0.05$, and as tendencies to differ in the corresponding indices at $p = 0.1–0.2$.

RESULTS

Immune status of Trakai district females. Comparing immunological indices of light alcohol users group (n = 136) and abstainers group (n = 11), the absolute quantity of monocytes (25%), the ratio of $CD4^+/CD8^+$ (17%) and the percentage index of blasttransformation (6%) were found to be lower in the former. Only the percentage of $CD8^+$ was higher by 20% (Tab 1–3).

It was not possible to make any comparisons due to a small number of females in other groups.

Immune status of Trakai district males. Only one abstainer was in the male group, so it was impossible to make any comparisons with other groups.

Comparing the haematological and immunological indices of moderate alcohol users males group (n = 51) and light alcohol users group (n = 29), the differences were not found.

A comparison of the data on alcohol abusers group (n = 46) with the same data on light alcohol users group (n = 29) showed that the percentage and absolute number of neutrophils (7% and 13%, respectively), IgG concentration in the blood serum (18%) of the former were lower. Higher were the lymphocyte percentage index (13%), the percentage of $CD4^+$ (8%) and blasts (4%) (Tables 1–3).

Table 1. *Leukocytes and indices of leukograms with reference to humans' place of residence, gender and alcohol consumption intensity*

District	Gender	Groups	n	Leukocytes n· 10^9/l	Lymphocytes		Monocytes		Neutrophils	
					%	n· 10^9/l	%	n· 10^9/l	%	n· 10^9/l
Trakai	Females	1	11	5.6±0.56	30±2.1	1.7±0.28	6±0.6	0.4±0.04●	60±2.2	3.3±0.30
		2	136	*●5.2±0.12	32±0.6	●*1.6±0.05	6±0.2	*0.3±0.01●	*60±0.7	*3.2±0.09
		3	5	6.5±0.84	38±4.3	2.5±0.39	3±0.6	0.2±0.06	56±4.5	3.6±0.52
		4	3	5.7±0.98	29±3.6	1.6±0.10	7±3.0	0.4±0.02	59±6.5	3.5±0.98
		5	144	5.3±0.12*	32±0.6	1.7±0.05	6±0.2	0.3±0.01*	60±0.6	3.2±0.09
	Males	1	1	-	-	-	-	-	-	-
		2	29	*■6.2±0.32	31±1.7■■	*2.0±0.17■■	6±0.6	*0.4±0.05	●61±2.1**	●*3.8±0.23●●
		3	51	5.9±0.23	31±1.1*	1.8±0.09**	7±0.5**	0.4±0.03	■60±1.1	3.6±0.19
		4	46	5.8±0.22	●●35±1.7*■■	2.0±0.08**	6±0.4**	0.4±0.03	■56±1.7**	3.3±0.18●●
		5	126	5.9±0.15	33±0.9	1.9±0.06	7±0.3	0.4±0.02	59±0.9	3.5±0.11
Širvintos	Females	1	27	6.0±0.32**	32±1.7	1.9±0.13	6±0.6	0.4±0.04*	60±2.0	3.7±0.24■■
		2	123	●5.6±0.14**	34±0.8	●1.9±0.06	6±0.3	0.3±0.02*	*57±0.9	3.3±0.11■■
		3	2	4.3±0.38	40±6.5	1.7±0.13	6±1.0	0.3±0.02	50±8.0	2.2±0.54
		4	1	-	-	-	-	-	-	-
		5	126	5.6±0.13	34±0.8	1.9±0.06	6±0.3	0.3±0.02	57±0.9	3.3±0.11
	Males	1	5	5.7±0.85	34±6.2	1.8±0.22	6±0.8	0.3±0.07	57±7.3	3.4±0.91
		2	39	■**5.3±0.25■■	*35±1.3**	1.8±0.07■■	7±0.6	●0.3±0.03■	●55±1.5*	●3.0±0.21**
		3	71	5.8±0.16■■	*31±1.0	1.8±0.07	7±0.3	0.4±0.02■	59±1.0*	3.4±0.13**
		4	14	**6.3±0.56	●●31±2.0**	1.9±0.22	6±0.8	●0.4±0.04*	59±2.6	3.8±0.44
		5	124	5.7±0.14	32±0.8	1.8±0.05	7±0.3	0.4±0.02*	58±0.8	3.3±0.11

1 – abstainers; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – all alcohol users.
*, ■, ● - $p \leq 0.05$; **, ■■, ●● - p = 0.1-0.2 (different symbols designate the compared groups).

When comparing immunological indices of alcohol abusers group (n = 46) and moderate alcohol users group (n = 51), the percentage indices of monocytes (14%) and neutrophils (7%), IgG concentration in blood serum (13%) were lower in the former. Other indices of the alcohol abusers were higher: the percentage and absolute quantity of lymphocytes (both by 11%), the percentage and absolute quantity of $CD4^+$ (8% and 14%, respectively) and the percentage index of blasts (4%) (Tables 1–3).

Immune status of Širvintos district females. When comparing immunological indices of light alcohol users group (n = 123) and abstainers group (n = 27), the absolute quantities of leukocytes (7%), monocytes (25%), neutrophils (11%), and PhN (1%) were lower in the former. However the percentage and absolute number of $CD8^+$ (11% and 20%, respectively), IgA concentration in blood serum (13%) were higher in the light alcohol users group (Tables 1–3).

Comparative analysis of other female groups was not performed because of a small number of females.

Immune status of Širvintos district males. It was impossible to do any comparisons with abstainers (n = 5) due to a small number of males in this group.

A comparison of the data on the moderate alcohol users group (n = 71) with the same data on the light alcohol users group (n = 39) showed that percentage of lymphocytes (11%) was lower in the former. Higher were the total number of leukocytes (9%), the absolute quantity of monocytes (33%), the percentage and absolute quantity of neutrophils (7% and 13%, respectively), the percentage of $CD4^+$ (8%), the ratio of $CD4^+/CD8^+$ (17%), the absolute quantity of $CD16^+$ (33%) and PhI (17%) (Tables 1–3).

The percentage index of lymphocytes was lower by 11% in Širvintos district alcohol abusers group (n = 14) in comparison with the same district light alcohol consumers group (n = 39). Higher were the total number of leukocytes (19%), the absolute quantity of monocytes, $CD4^+$ and $CD16^+$ (33%, 14% and 33%, respectively) (Tables 1, 2).

The same comparative analysis showed that PhI (14%) and IgG concentration (10%) were smaller in alcohol abusers group (n = 13) than analogous indices in group of moderate alcohol consumers (n = 70). Higher was absolute quantity of $CD4^+$ (14%) (Tables 2, 3).

Immune status of Trakai district males and females. It was impossible to make any comparisons in females (n = 11) and males (n = 1) abstainers groups.

When comparing the haematological and immunological indices of light alcohol consumption between males (n = 29) and females (n = 136), we found that the total number of leukocytes (19%), the absolute number of lymphocytes (25%), monocytes (33%), neutrophils (18%), $CD5^+$ (20%), $CD4^+$ (14%), the percentage index of $CD72^+$ (20%) and IgA concentration in the blood serum (17%) were higher in the former (Tables 1–3).

Immune status of Širvintos district males and females. Comparison between male (n = 5) and female (n = 27) groups not using alcohol was not performed, due to a small number of males in abstainers group.

Comparing the haematological and immunological indices of light alcohol consumption between males (n = 33) with the same group of females (n = 110), the absolute quantity of $CD5^+$ (8%), the percentage index and absolute quantity of $CD4^+$ (7% and 12% respectively), the ratio of $CD4^+/CD8^+$ (14%) and IgM concentration in blood serum (9%) were lower in the former (Tables 2, 3). Other indices did not differ.

Table 2. *T, B and NK lymphocyte populations with reference to humans' place of residence, gender and alcohol consumption intensity*

District	Gender	Groups	n	T ($CD5^+$)		$CD4^+$		$CD8^+$		$CD4^+/CD8^+$	B ($CD72^+$)		NK ($CD16^+$)	
				%	n· 10^9/l	%	n· 10^9/l	%	n· 10^9/l		%	n· 10^9/l	%	n· 10^9/l
Trakai	Females	1	10	61±2.7	1.1±0.21	45±2.2	0.8±0.13	25±1.8*	0.5±0.11	1.8±0.14*	10±1.8	0.2±0.05	19±2.0	0.4±0.09
		2	125	61±0.7	●1.0±0.03**	42±0.7	*0.7±0.03●●	30±0.6*	■0.5±0.02	1.5±0.05*	10±0.5■■	0.2±0.01	●21±0.7	*0.3±0.02
		3	2	56±2.5	1.7±0.43	41±3.0	1.3±0.35	23±3.0	0.7±0.23	1.8±0.10	10±1.5	0.3±0.01	11±3.0	0.3±0.02
		4	2	64±0.5	1.0±0.12	46±6.0	0.7±0.17	22±6.5	0.3±0.06	2.3±0.94	8±1.0	0.2±0.03	19±1.0	0.3±0.05
		5	129	61±0.7	1.0±0.03	42±0.7	0.7±0.03	30±0.6	0.5±0.02	1.5±0.05	10±0.5	0.2±0.01	21±0.7	0.3±0.02
	Males	1	1	-	-	-	-	-	-	-	-	-	-	-
		2	26	62±1.3	1.2±0.11**	●●40±1.2	0.8±0.07●●	30±1.4	0.6±0.08	●●1.4±0.08	12±1.0■■	0.2±0.03	21±1.1	●*0.4±0.04
		3	49	62±1.2	1.1±0.06	40±1.2**	0.7±0.04**	31±1.2	0.6±0.04	1.4±0.09	**12±1.0	0.2±0.03	21±1.3	0.4±0.03
		4	41	63±1.2	1.2±0.06	●●43±1.2**	0.8±0.04**	32±1.5	0.6±0.05	1.5±0.08	10±1.0	0.2±0.02	20±1.3	0.4±0.03
		5	116	62±0.7	1.2±0.04	41±0.7	0.8±0.03	31±0.8	0.6±0.03	1.4±0.05	11±0.6	0.2±0.02	20±0.7	0.4±0.02
Širvintos	Females	1	27	62±1.7	1.2±0.09	43±1.9	0.8±0.07	28±1.4●●	0.5±0.05*	1.6±0.14	12±1.4	0.2±0.03	18±1.4	0.3±0.04
		2	110	61±0.7	●1.2±0.04●●	*41±0.8	■*0.8±0.02	31±0.7●●	■0.6±0.02*	●●1.4±0.05	10±0.6	0.2±0.01	●18±0.6	0.3±0.02
		3	2	59±7.0	1.0±0.05	41±1.0	0.7±0.03	21±7.0	0.4±0.09	2.2±0.68	9±4.0	0.2±0.08	18±8.0	0.3±0.12
		4	1	-	-	-	-	-	-	-	-	-	-	-
		5	113	61±0.7	1.2±0.04	41±0.7	0.8±0.02	30±0.7	0.6±0.02	1.4±0.05	10±0.5	0.2±0.01	18±0.6	0.3±0.02
	Males	1	5	59±3.4	1.0±0.15	37±5.4	0.7±0.14	30±3.0	0.5±0.03	1.2±0.23	13±1.7	0.2±0.03	15±1.3	0.3±0.03
		2	33	61±1.5	1.1±0.05●●	*38±1.5■■	■0.7±0.03■■	32±1.3	0.6±0.03	●●1.2±0.08*	11±0.9	0.2±0.02	19±1.3	●0.3±0.02*■■
		3	62	61±0.9	1.1±0.06	41±0.9■■	●●0.7±0.03	31±0.9	0.6±0.03	1.4±0.06*	**10±0.5	0.2±0.01	20±0.8	0.4±0.02*
		4	14	62±2.0	1.2±0.14	41±1.6	●●0.8±0.07■■	30±1.9	0.6±0.07	1.4±0.11	12±1.7	0.2±0.06	20±2.0	0.4±0.05■■
		5	109	61±0.7	1.1±0.04	40±0.7	0.7±0.03	31±0.7	0.6±0.02	1.4±0.04	10±0.5	0.2±0.01	20±0.6	0.4±0.01

1 – abstainers; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – all alcohol users.
*, ■, ● - p≤0.05; **, ■■, ●● - p=0.1-0.2 (different symbols designate the compared groups).

Table 3. *Blasttransformation, phagocytic activity of neutrophils and concentration of immunoglobulins with reference to humans' place of residence, gender and alcohol consumption intensity*

District	Gender	Groups	n	Blasts %	n	PhN %	PhI	n	Ig (g/l)		
									IgG	IgA	IgM
Trakai	Females	1	11	77±2.7**	9	98±0.6	6.2±0.42	11	10.4±0.68	1.7±0.20	1.2±0.15
		2	128	72±0.8**	132	97±0.3	6.0±0.15	133	10.4±0.27	*1.8±0.08	*1.2±0.04
		3	5	70±4.6	4	97±0.5	4.4±0.09	5	9.2±0.68	1.7±0.30	1.2±0.08
		4	3	68±10.0	3	99±0.7	5.6±0.24	3	13.4±2.3	1.7±0.48	2.2±0.49
		5	136	72±0.8	139	97±0.3	5.9±0.15	141	10.4±0.26	1.8±0.07	1.3±0.04
	Males	1	1	-	1	-	-	1	-	-	-
		2	25	72±1.4●●	27	96±1.5	5.6±0.32	28	11.4±0.60*	*2.1±0.13	1.2±0.12
		3	46	■■72±1.3	47	97±0.8	6.2±0.23	50	●10.8±0.42	●●2.2±0.13	■1.2±0.06
		4	46	■■75±1.1●●	44	98±0.4	6.0±0.30	46	●9.4±0.29*	2.2±0.14	1.1±0.06
		5	117	73±0.7	118	97±0.5	6.0±0.16	124	10.4±0.25	2.2±0.08*	1.2±0.04
Širvintos	Females	1	25	73±1.5	26	98±0.4**	6.2±0.33	26	10.3±0.47	1.5±0.10**	1.2±0.06
		2	115	73±0.7	120	97±0.4**	5.8±0.17	119	10.3±0.24	1.7±0.05**	*1.1±0.03●●
		3	2	72±0.0	1	-	-	2	9.4±2.3	2.4±0.75	1.2±0.40
		4	1	-	1	-	-	1	-	-	-
		5	118	72±0.7	122	97±0.4	5.8±0.16	122	10.3±0.23	1.7±0.05	1.1±0.03
	Males	1	5	70±1.6	5	97±1.0	5.7±0.78	5	10.5±0.41	1.8±0.28	1.2±0.21
		2	34	73±1.4	39	96±0.8	5.3±0.29*	36	10.0±0.39	1.9±0.13	1.0±0.05●●
		3	70	73±0.9	69	97±0.6	●6.2±0.23*	68	10.6±0.35*	●●1.9±0.09	■1.0±0.04
		4	13	71±2.4	14	97±0.6	●5.3±0.36	13	9.5±0.40*	2.1±0.36	1.0±0.05
		5	117	73±0.7	122	96±0.4	5.8±0.17	117	10.3±0.24	1.9±0.08	1.0±0.03

1 – abstainers; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – all alcohol users.
*, ■, ●, - p≤0.05; **, ■■, ●● - p=0.1-0.2 (different symbols designate the compared groups).

There was a low number of females in alcohol abusers (n = 1) and light alcohol consumers (n = 2) groups, so the comparison with the same groups of males was not performed.

Immune status of Trakai and Širvintos district females. When comparing the immunological parameters of Trakai district female light alcohol consumer group (n = 136) with the same Širvintos district women group (n = 123), the total number of leukocytes (7%), absolute quantity of lymphocytes (16%), $CD5^+$ (17%), $CD4^+$ (12%) and $CD8^+$ (17%) were lower in the former. The higher were the percentage index of neutrophils (5%), $CD16^+$ (17%) and IgM concentration in blood serum (9%) (Tables 1–3).

Immune status of Trakai and Širvintos district males. When comparing the indices of light alcohol consumption in group of males in Trakai (n = 29) with the same in Širvintos district (n = 39) the total number of leukocytes (17%), absolute quantity of lymphocytes (11%), the percentage and absolute number of neutrophils (11% and 27%, respectively), the ratio of $CD4^+/CD8^+$ (17%) and absolute number of $CD16^+$ (33%) were found to be higher in the former group (Tables 1, 2).

A comparison of the data in the Trakai district moderate alcohol consumption group (n = 49) with the same data in Širvintos district (n = 62) showed that the percentage index of $CD72^+$ (20%), IgA and IgM concentration in blood serum (16% and 20% respectively) were higher in the former (Tables 2–3).

The immunological parameters of alcohol abusers in Trakai (n = 46) and Širvintos (n = 14) districts differed insignificantly. Only percentage index of lymphocytes (13%) was higher in Trakai district group.

DISCUSSION AND CONCLUSIONS

Millions of tons of harmful gases and particles are released into the air each year. People exposed to air pollutants have an increased danger to experience serious health effects. These health effects can include damage to immune system too (3, 9, 13). The literature suggests that also alcohol type and consumption intensity differently affect immune system functions in men and women (5, 6).

However, most studies have not considered the combination impact of environmental contamination, gender and bad habits on human immunoreactivity.

This study has contributed to the process of evaluating the disturbance of human immunity in respect to all earlier mentioned factors. Because of biological differences, women appear to become more afflicted than men after drinking equivalent amounts of alcohol (14).

Our investigations showed that light alcohol consumption within the female groups of Trakai and Širvintos districts causes similar alterations of immune system functions in comparison with abstainers groups. In women, the possibility to detect association with high dose of alcohol intake was limited because of a limited range of alcohol intake.

The obtained data showed that in Trakai district immune parameters of moderate alcohol users male group in comparison with light alcohol users did not differ. In the group of males who were using alcohol more intensively (alcohol abusers), stimulation of immunity was poorly expressed and at the same time negligible

immunosuppression in comparison with light and moderate alcohol consumption groups of males started to occur. In relatively clean Širvintos area the moderate use of alcohol caused emphasized stimulation of immune indices in comparison with the light alcohol users male group. In this district, immune indices stimulation in alcohol abusers male group was less expressed in comparison with light alcohol consumption male group.

In the light alcohol users female group, reduction of some parameters of cellular immunity in polluted Trakai area, as compared with parameters of female living in relatively clean Širvintos area, was noted. Also the stimulation of some other immune system functions was expressed in Trakai district.

The immunity parameters of light alcohol users male group from the Trakai area were stimulated in comparison with parameters of the same male group living in Širvintos area. In the moderate alcohol users male group stimulation of immune functions was expressed less at the same comparison.

The immune system parameters in the light alcohol users male group of Trakai area were higher in comparison with the similar female group in the same area. On the other hand parameters of immunity observed in male light drinkers of Širvintos area were weaker compared with parameters of the light female alcohol users group of the same district.

In conclusion, our research showed various immunomodulations in male and female that depended on the intensity of alcohol consumption and place of residence.

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