

DISTURBANCE OF HUMAN IMMUNOHOMEOSTASIS BY ENVIRONMENTAL POLLUTION AND ALCOHOL CONSUMPTION

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Environmental pollution and consumption of alcohol evoke various immuno-modulations promoting the progress of different pathologies. The purpose of this study was to evaluate the influence of alcohol consumption intensity on the immune system functions of humans living in ecologically different regions, i.e. in a district polluted with industrial siftings (Trakai, n=270) and in a relatively clean district (Širvintos, n=250). In the Trakai cohort 96% and in Širvintos group 89% of persons consumed alcohol. With regard to alcohol consumption habits the immunohaematological indices were investigated in the following four groups: abstinents, light alcohol users, moderate alcohol users and alcohol abusers. We determined the compensatory mechanisms of immune system functions of moderate alcohol users and alcohol abusers in comparison with abstinents in the relatively clean Širvintos district. In the Trakai district polluted with industrial siftings such compensatory reactions were not found. Thus, damage to the immune system functions is not only an endogenous risk factor for many diseases, but also an indicator of organism injury. This investigation stated, that immunity disturbance in humans depends on alcohol consumption intensity and place of residence.

Keywords: immunity, alcohol consumption intensity, environmental contamination

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Introduction

The main role of the immune system is to maintain homeostasis and sustain host defence. Environmental pollution with industrial siftings influences functions of the human organism and is associated with various changes in the inner medium.

Disbalance of immune functions as a stress factor for the homeostasis of the organism is very important. The influence of industrial pollutants and other harmful factors exhaust the protective powers of the organism and impairs its immunity. Extensive evidence has been accumulated on the health-related effects of air pollution, which induces impairment of chronic respiratory and cardiovascular diseases, alteration of host defenses and possibly contributes also to cancer development, etc. [1–3].

Alcohol consumption in the long run damages the organism and may evoke several diseases. Alcoholic drinks damage the organism not only by the ethanol itself, but also by the substances formed during its metabolism. The effect of alcohol depends on the type of drink (beer, wine or spirits). Alcohol consumers may differ in other aspects of their lifestyle and thereby they can be at different stages of development of their disease [4–6]. The damage of the organism's somatic cells may alter various functions of the immune and other systems. Even acute, moderate alcohol consumption modulates the strength of immune functions that may further contribute to the reduction of immunity and host defense [7]. Alcohol exerts a variety of short and long-term effects on cell mediated and humoral immune response. Decreased antigen presenting cell function appears to be a key element in the ethanol induced reduction of cell-mediated immunity [8, 9].

This work is the continuation of a series of publications with the framework of the state scientific program "Ecological sustainability of regional development in a historical perspective: Lithuanian case studies" (1992–1997). Studies about the dependence of human immunity on environmental pollution, age, gender, and the changes of humans' immune state with respect to tobacco smoking and cancer risk were already published [10–12].

Our earlier investigations showed that the immune state of alcohol users depended on the place of residence and gender [13]. Therefore we considered it purposeful to elucidate whether alcohol consumption (amount and frequency) may lead to some immunomodulation. Therefore, the aim of this study was to assess the influence of alcohol consumption (amount and frequency) on the immunohomeostasis of humans living in ecologically different regions, i.e. in a district contaminated with industrial siftings (Trakai) and in a relatively clean district (Širvintos).

Materials and methods

The immune state was investigated in 270 humans (126 males and 144 females) who lived in a contaminated district (Trakai) and in 250 humans (124 males and 126 females) who lived for many years in a conventionally clearer district (Širvintos). The age of the individuals was 20–64 years. In the Trakai cohort 96% of persons (99% of males and 93% of females) and in Širvintos 89% (96% of males and 82% of females) regularly consumed alcohol. With reference to the strength of alcoholic beverages and alcohol consumption frequency the immuno-haematological indices were investigated in the following four groups:

- 1) abstinents,
- 2) light alcohol users (wine or beer rarely),
- 3) moderate alcohol users (1–3 times per month not less than 250 g of spirits),
- 4) alcohol abusers (once or more per week more than 250 g of spirits).

The indices of cellular immunity determined for all the investigated persons were the following: total leukocyte number, lymphocyte, monocyte and neutrophil percentage and absolute number, total T lymphocyte population ($CD5^+$), T helpers ($CD4^+$), T cytotoxic/ suppressors ($CD8^+$), immunoregulation index ($CD4^+/CD8^+$), B lymphocytes ($CD72^+$), NK cells ($CD16^+$) (Sorbent, Russia). Percentage rate and absolute number of lymphocyte populations and subpopulations were also determined. In addition, to evaluate the immune state, 2 indices of blood neutrophils' phagocytic activity (phagocytosis index – PhI and phagocytosis number – PhN) were employed. To evaluate the humoral immunity concentrations of IgG, IgA and IgM (N. F. Gamaleya Institute of Epidemiology and Microbiology of Academy of Medical Sciences, Russia) in blood serum were studied. The leukocyte formula was determined. The investigations were carried out by routine laboratory methods [14].

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

Results

Trakai district. A comparison of the immunological indices of Trakai district light alcohol users and abstinent showed a tendency of a decrease in the immunoregulatory $CD4^+/CD8^+$ index (17%) and PhN (1%) and a markedly higher rate of $CD8^+$ (15%) in the former group (Tables II, III).

While comparing the immunological indices of moderate alcohol consumers with those of abstinent in the former the rate of $CD4^+$ tended to be lower (9%), the immunoregulatory index $CD4^+/CD8^+$ was essentially lower (22%), and the incidence of $CD8^+$ cells tended to be higher (15%). IgA concentration in the blood serum was reliably higher (29%) (Tables II, III).

While comparing data on alcohol abusers and abstinent, a tendency to a lower $CD4^+/CD8^+$ index (by 17%), a markedly higher $CD8^+$ rate (by 19%) and a tendency to a higher IgA concentration in blood serum (by 23%) were found (Tables II, III).

Some cellular immunity indices of the Trakai cohort, independently of alcohol consumption level, were lower than the analogous indices in the abstinent group. The immunoregulatory $CD4^+/CD8^+$ index was reliably lower (by 17–22%). The $CD8^+$ rate was higher (by 15–19%) in all three groups (light and moderate alcohol users, alcohol abusers) in comparison to the same indices of abstinent.

Širvintos district. When comparing the haematological and immunological indices of light-alcohol users with the same indices of abstinent, the following indices showed a tendency to be lower in the former: the absolute monocyte (25%) and $CD4^+$ counts (12%), the PhI (8%), PhN (1%). The absolute quantity of $CD8^+$ was higher (20%) and IgA concentration in blood serum had a tendency to be higher by 6% (Tables I, II, III). In moderate alcohol consumers the absolute quantity of $CD4^+$ had a tendency to be lower (by 12%) in comparison with the analogous index in abstinent ($n=32$). Also the IgM concentrations in their blood sera were essentially lower (by 17%). The percentage of monocytes, the absolute quantity of $CD16^+$ and the IgA concentration in the blood serum were higher by 17%, 33% and 19%, respectively (Tables I, II, III).

In Širvintos district alcohol abusers, the phagocytosis index (PhI) and IgM concentration in blood serum had a tendency to be lower (by 13% and 17%) than the same indices in abstinent, but the absolute number of $CD16^+$ and the percentage of monocytes had a tendency to be higher (by 33% and 17%, respectively).

In Širvintos district immunostimulation was more pronounced in moderate alcohol consumers than in the abstinent. The absolute quantity of $CD16^+$, IgA concentration in blood serum and the rate of monocytes were also higher (by 30%, 19% and 17%, respectively).

Table I
Leukocytes and indices of leukograms with reference to humans place of residence and alcohol consumption intensity

District	Groups	n	Leukocytes		Lymphocytes		Monocytes		Neutrophils	
			n·10 ⁹ /l	%	n·10 ⁹ /l	%	n·10 ⁹ /l	%	n·10 ⁹ /l	%
Trakai	1	12	5.8±0.57	32±2.2	1.9±0.31	7±0.8	0.4±0.08	59±2.5	3.3±0.27	
	2	165	5.4±0.12	32±0.6	1.7±0.05	6±0.2	0.3±0.01	60±0.6	3.3±0.09	
	3	56	5.9±0.23	32±1.1	1.9±0.09	7±0.5	0.4±0.03	60±1.1	3.6±0.18	
	4	49	5.8±0.21	34±1.6	1.9±0.08	6±0.4	0.4±0.03	57±1.6	3.3±0.18	
	5	270	5.6±0.10	32±0.5	1.8±0.04	6±0.2	0.4±0.01	59±0.6	3.3±0.07	
Širvintos	1	32	6.0±0.30	32±1.7	1.9±0.11	6±0.5**	0.4±0.04*	59±2.0	3.6±0.24	
	2	162	5.6±0.12	34±0.6	1.9±0.05	6±0.2	0.3±0.01*	60±0.8	3.2±0.10	
	3	73	5.7±0.16	31±1.0	1.8±0.07	7±0.3**	0.4±0.02	59±1.0	3.4±0.12	
	4	15	6.1±0.56	31±2.0	1.9±0.22	7±0.2**	0.4±0.03	59±2.4	3.7±0.42	
	5	250	5.7±0.10	33±0.5	1.8±0.04	6±0.2	0.3±0.01	57±0.6	3.3±0.08	

1 – abstinent; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – total

* p≤0.05; ** p=0.1–0.2.

Table II
T, B and NK lymphocyte populations with reference to humans place of residence and alcohol consumption intensity

District	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	%	n·10 ⁹ /l
Trakai	1	11	61±2.5	1.2±0.21	44±2.2**	0.8±0.12	*26±1.9**	0.5±0.13	**1.8±0.15*	12±2.0	0.2±0.07	19±1.8	0.4±0.09	
	2	151	61±0.6	1.0±0.03	42±0.6	0.7±0.02	*30±0.6	0.5±0.02	**1.5±0.04	11±0.5	0.2±0.01	21±0.6	0.4±0.02	
	3	51	62±1.2	1.2±0.06	40±1.2**	0.7±0.04	30±1.2**	0.6±0.04	1.4±0.09*	12±1.0	0.2±0.03	20±1.2	0.4±0.03	
	4	43	63±1.1	1.2±0.06	43±1.2	0.8±0.04	*31±1.4	0.6±0.05	**1.5±0.09	10±0.9	0.2±0.02	20±1.2	0.4±0.03	
	5	245	61±0.5	1.1±0.03	42±0.5	0.7±0.02	30±0.5	0.5±0.02	1.5±0.03	11±0.4	0.2±0.01	21±0.5	0.4±0.01	
Širvintos	1	32	61±1.5	1.2±0.08	42±1.8	0.8±0.06**	29±1.2	0.5±0.04*	1.5±0.12	12±1.2	0.2±0.03	18±1.2	**0.3±0.04*	
	2	143	61±0.6	1.1±0.03	40±0.7	0.7±0.02**	31±0.6	0.6±0.02*	1.4±0.04	11±0.5	0.2±0.01	19±0.6	0.3±0.01	
	3	64	61±0.9	1.1±0.06	41±0.9	0.7±0.03**	31±0.9	0.5±0.03	1.4±0.06	10±0.5	0.2±0.01	20±0.8	0.4±0.02*	
	4	15	62±1.9	1.1±0.13	41±1.4	0.7±0.07	30±1.8	0.6±0.06	1.4±0.11	11±1.6	0.2±0.06	20±1.9	**0.4±0.05	
	5	232	61±0.5	1.1±0.03	40±0.5	0.7±0.02	31±0.5	0.6±0.02	1.4±0.03	10±0.3	0.2±0.01	19±0.4	0.3±0.01	

1 – abstinent; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – total

* p≤0.05; ** p=0.1–0.2.

Table III
Phagocytic activity of blood neutrophils and concentration of immunoglobulins in blood serum with reference to humans place of residence and alcohol consumption intensity

District	Groups	n	PhN (%)	PhI	n	Ig (g/l)		
						IgG	IgA	IgM
Trakai	1	10	98±0.5**	6.1±0.39	12	10.2±0.65	**1.7±0.18*	1.2±0.14
	2	159	97±0.4**	5.9±0.14	161	10.6±0.25	1.9±0.07	1.2±0.04
	3	51	97±0.8	6.1±0.22	55	10.7±0.39	2.2±0.12*	1.2±0.06
	4	47	98±0.4	6.0±0.28	49	9.6±0.33	**2.1±0.14	1.1±0.07
	5	257	97±0.3	6.0±0.11	265	10.4±0.18	2.0±0.06	1.2±0.03
Širvintos	1	31	97±0.4*	6.2±0.30**	31	10.4±0.40	**1.6±0.10*	1.2±0.06*
	2	159	96±0.3*	5.7±0.15**	155	10.2±0.20	**1.7±0.05	1.1±0.03
	3	70	97±0.6	6.2±0.23	70	10.6±0.35	1.9±0.09*	1.0±0.04*
	4	15	97±0.6	5.4±0.35**	14	9.8±0.50	2.1±0.33	1.0±0.05*
	5	254	96±0.3	5.8±0.11	249	10.3±0.16	1.8±0.05	1.1±0.02

1 – abstinent; 2 – light alcohol users; 3 – moderate alcohol users; 4 – alcohol abusers; 5 – total

* $p \leq 0.05$; ** $p = 0.1-0.2$.

Discussion

A reduced immunoregulatory $CD4^+/CD8^+$ ratio and upregulated $CD8^+$ index were characteristic of all three alcohol consumption groups of the Trakai cohort in comparison with the abstinent. Recent investigations have shown that $CD8^+$ cells fulfil not only cytotoxic but also immune response suppressing functions [15].

Our results showed that some cellular immunity indices of Širvintos district inhabitants were more sensitive to the influence of light alcoholic beverages than those of abstinent in comparison with the same data on the Trakai cohort. Light alcohol consumption triggered a decrease of four indices (monocytes, $CD4^+$, PhI, PhN) in the Širvintos cohort whereas moderate alcohol consumption and excessive drinking provoked a reduction of two indices ($CD4^+$ and IgM). However, in the two latter groups, which preserved immune homeostasis, also compensatory mechanisms (increased number of monocytes, $CD16^+$ cells and IgA concentration in the blood serum) were revealed.

Our earlier investigations showed that the immune functions of alcohol consumers (without reference to alcohol amount and frequency) from a district contaminated with industrial siftings (Trakai) was stimulated more strongly in comparison with the immune functions of the matched cohort from a relatively non-contaminated (Širvintos) district. However the immunocompetence of abstinent living in ecologically different regions practically did not differ [13]. We explained this fact by the influence of tobacco smoking. Previous data showed that the immune functions in smokers of both Trakai and Širvintos districts were enhanced in comparison with the same functions of non-smokers from both districts. Stimulation of the functions of the immune system was however more evident among smokers from Trakai district. On the other hand, there was suppressive impact of environmental contamination with industrial siftings on the immune system of Trakai district non-smokers revealed in comparison with the same functions of non-smokers from Širvintos district [11]. Therefore immunity differences between the Trakai and Širvintos cohorts may be determined by such immunomodulatory factors as environmental pollution and tobacco smoking. The impact of these factors disturbs the immune functions of Trakai district inhabitants, therefore their immune reactions to alcohol consumption amount and frequency may differ from the same reactions of this relatively clean Širvintos district inhabitants.

The risk of many diseases increases when alcohol consumption is combined with cigarette smoking. Heavy drinkers frequently are heavy smokers, and are exposed to a higher risk of upper digestive tract cancer and other pathologies [16].

Deleterious effects of alcohol consumption on the immune system and its disturbance may be an endogenous risk factor for the development of many diseases.

In conclusion, our data demonstrated that the reaction of immune functions to alcohol consumption amount and frequency is different in people living in regions with different levels of industrial pollution. We detected the compensatory mechanisms of immune functions in the relatively clean Širvintos district in a cohort of moderate alcohol users and alcohol abusers. However in the cohort from a district contaminated with industrial siftings no such mechanisms were elucidated.

References

1. Brunekreef, B., Holgate, S. T.: Air pollution and health. *Lancet* **360(9341)**, 1233–1242 (2002).
2. Lagorio, S., Forastiere, F., Lipsott, M., Menichini, E.: Air pollution from traffic and the risk of tumors. *Ann Ist Super Sanita* **36(3)**, 311–329 (2000).
3. Nafstad, P., Haheim, L. L., Oftedal, B., Gram, F., Holme, J., Hjermann, I., Leren, P.: Lung cancer and air pollution: a 27 year follow up of 16,209 Norwegian men. *Thorax* **58(12)**, 1071–1076 (2003).
4. Poschl, G., Seitz, H. K.: Alcohol and cancer. *Alcohol Alcohol* **39(3)**, 155–165 (2004).
5. Castellsague, X., Quintana, M. J., Martinez, M. C., Nieto, A., Sanchez, M. J., Juan, A., Mounier, A., Carerra, M., Agudo, A., Quer, M., Munoz, N., Hererro, R., Franceshi, S., Bosch, F. X.: The role of type of tobacco and type of alcoholic beverage in oral carcinogenesis. *Int J Cancer* **108(5)**, 741–749 (2004).
6. Prescott, E., Gronback, M., Becker, U., Sorensen, T. I.: Alcohol intake and the risk of lung cancer: influence of type of alcoholic beverage. *Am J Epidemiol* **149(5)**, 463–470 (1999).
7. Szabo, G.: Monocytes, alcohol use, and altered immunity. *Alcohol Clin Exp Res* **22(5)**, 216–219 (1998).
8. Diaz, L. E., Montero, A., Gonzalez-Gross, M., Vallejo, A., Romeo, J., Marcos, A.: Influence of alcohol consumption on immunological status: review. *Eur J Clin Nutr* **56(3)**, 50–53 (2002).
9. Szabo, G.: Consequences of alcohol consumption on host defense. *Alcohol Alcohol* **34(6)**, 830–841 (1999).
10. Kazbarienė, B., Kemeklienė, R., Šukytė, Z., Moncevičiūtė-Eringienė, E.: Human immunodeficiency reactions to environmental contamination. Part 5. *Acta Medica Lituanica* **3**, 213–219 (1998).
11. Kazbariene, B., Kemekliene, R., Krikštaponiene, A., Sigliukiene, Dž., Moncevičiūtė-Eringienė, E.: The immune state of humans with respect to tobacco smoking. Part 1. *Acta Medica Lituanica* **7(1)**, 41–44 (2000).
12. Kazbarienė, B., Kemeklienė, R., Krikštaponienė, A., Sigliukienė, Dž., Moncevičiūtė-Eringienė, E.: The immune state of humans with respect to tobacco smoking. Part IV. *Acta Medica Lituanica* **8**, 147–151 (2001).

13. Kazbariene, B. A., Krikstaponiene, A. S., Monceviute-Eringiene, E. V.: Immune state of humans with respect to alcohol consumption and cancer risk. *Exp Oncol* **24(4)**, 308–311 (2002).
14. Monceviute-Eringiene, E., Kazbariene, B., Milashiene, V. E., Kemekliene, Characiejus, D., Levit, L.: Evaluation of compensatory reactions with the use of enterobacterial antigens upon suppressed immune function. *Immunolog* **6**, 48–51 (1991) (in Russian).
15. Filaci, G., Fravega, M., Negrini, S., Procopio, F., Fenoglio, D., Rizzi, M., Brenci, S., Contini, P., Olive, D., Ghio, M., Setti, M., Accolla, R. S., Puppo, F., Indiveri, F.: Nonantigen specific CD8⁺ T suppressor lymphocytes originate from CD8⁺ CD28⁻ T cells and inhibit both T-cell proliferation and CTL function. *Hum Immunol* **65(2)**, 142–156 (2004).
16. Gronbaek, M., Becker, U., Johansen, D., Tonnesen, H., Jensen, G., Sorensen, T. I.: Population based cohort study of the association between alcohol intake and cancer of the upper digestive tract. *BJM* **317(7162)**, 844–847 (1998).