The Immune State of Humans with respect to Tobacco Smoking. Part 3

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Smoking is a cause of various immunomodulations, tumours and other diseases, which might depend on the duration of the contact with tobacco smoke and its intensity .

The total number of persons under investigation comprised 564: smokers in the contaminated Trakai district (n = 282) comprised 41% and in the slightly contaminated Širvintos district (n = 282) 36%. With respect to smoking, the indices were investigated in the following four groups: 1) non-smokers; 2) light smokers (1–10 cigarettes /24 h); 3) moderate smokers (11–20 cigarettes / 24 h); 4) heavy smokers (more than 20 cigarettes / 24 h).

The activity of the immune system of the organism was found to depend on the number of cigarettes smoked per 24 hours. The immunosupressive impact of chemical matters caused by tobacco smoke was identified by comparing the immunological indices of those who smoked 11–20 and 1–10 cig. / 24 h in the contaminated Trakai district (their leukocytes, neutrophils, CD4 and CD16 were lower). No differences were identified in the matched groups of the slightly contaminated Širvintos district.

Key words: immunological indices, immunostimulation, immunosuppression, environmental contamination, smoking intensity

INTRODUCTION

One of the most important cancer prevention objectives is the struggle against smoking, since it is a significant factor in the etiology of malignant tumour and other diseases [1, 2]. Moreover, during the recent years a huge impact of smoking was being recurrently demonstrated in the etiology of pulmonary cancer [3]. The ability to detect immune stimulation may be important in the assessment of lung cancer and various carcinogenic exposures. So, significantly higher than normal interleukin-2 receptor (IL-2R) levels were found in light, moderate and heavy smokers. Patients with lung cancer had serum levels of soluble IL-2R higher than both smokers and non-smokers [4].

Hydroquinone (HQ) is a major metabolite of benzene and is present in large quantities in cigarette tar as a result of the combustion of tobacco leaf pigments. Le Q et al. hypothesize that the immunosuppressive effects of cigarette smoking are due, in part, to the deposition of large quantities of HQ in the lungs .Their observations demonstrate that HQ, in concentrations comparable to those found in cigarette tar, is a potent inhibitor of IL-2 dependent T-cells proliferation and may therefore help to explain the potent immunosuppresive effect of cigarette smoke on lung T lymphocytes [5].

Our previous investigations have shown that the alterations or derangements of the functions of the immune system in tobacco smokers depende also on the environment [6] and gender [7]. The purpose of this work is to analyse changes in human immune reactivity in districts with different levels of different contamination by industrial siftings (Trakai – a contaminated district and Širvintos – a relatively non-contaminated district) with respect to tobacco smoking intensity.

MATERIALS AND METHODS

Investigations have been carried out in two regions: Trakai (contaminated by industrial siftings n = 282) and Širvintos (ecologically less contaminated, n = 282).

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The study cohort comprised 564 subjects: in Trakai district smokers comprised 41% and in Širvintos district 36%.

With respect to smoking, the indices were investigated in the following four groups: 1) non-smokers; 2) light smokers (1–10 cigarettes per day); 3) moderate smokers (11–20 cigarettes per day); 4) heavy smokers (more than 20 cigarettes per day).

Methods. All subjects were examinated according to the following cellular immunity indices: the total number of leukocytes, lymphocyte and monocyte percentage and absolute number, total T lymphocyte population (CD5), T helpers (CD4), suppressors (CD8), immunoregulatory index (CD4/CD8), B lymphocytes (CD72), NK cells (CD16). The percentage and absolute quantities of lymphocyte populations and subpopulations were counted. Besides, the blasttransformation reaction, two migration indices (MI) of leukocyte migration inhibition reaction (LMIR) and two indices of phagocytosis reaction (phagocytosis index PhI and phagocytosis number PhN) were used to evaluate the immune state. To evaluate humoral immunity, IgG, IgA, and IgM concentrations in the blood serum were examined. The leukocyte formula was determined. The laboratory investigations were based on generally accepted methods [8].

The data were evaluated employing the EXCEL program (version 5) in accordance with the Confidence Interval Analysis method.

RESULTS

The immune state of humans with respect to their place of residence and smoking intensity

Trakai district. When comparing the immunological indices of light smokers of Trakai district (n = 67) with the immunological indices of non-smokers (n = = 167), the quantity of leukocytes in the first ones was reliably higher (by 19%); the absolute quantity of lymphocytes was higher by 25%, monocytes – 33%, neutrophils – 19%, CD5 – 20%, CD4 – 28%, CD8 – 20%, CD16 – 33%, the percentage index of monocytes by 17%, CD72 – 20%; IgA concentration in blood serum was higher by 10%. The index of LMIR under 75% ECA concentration was lower (by 20%), i. e. sensibilisation of leukocytes against the antigen under investigation was higher. A reliably lower was the percentage index of monocytes (by 14%) and PhN (by 2%) (Tables 1–3).

Comparing the immunological indices of moderate smokers in Trakai district (n = 42) with the above indices of non smokers (n = 167) of the same region, the total number of leukocytes of the first ones was higher by 9%, the percentage index of lymphocytes by 10%. Reliably higher were absolute quantities of lymphocytes and monocytes (respectively by 19% and 33%), the percentage of CD5 index by 8%, CD5 absolute quantity by 20%, absolute CD4 and CD8 quantities were higher by 14% and 20% respectively and the percentage of CD72 index – by 20%. Reliably lower was the percentage of neutrophils (by 5%), CD16 (14%), PhN (1%) (Tables 1–3).

Comparing the immunological indices of moderate smokers (n = 42) of Trakai district with the indices of light smokers (n = 67) of the same district, the percentage of monocytes of the first ones had a tendency to be higher (by 17%) and the percentage of CD5 index was reliably higher (by 8%). The total number of leukocytes was lower by 8%, the absolute quantities of neutrophils by 11%, CD4 – 11%, the percentage of CD16 – 14% and their absolute quantity – by 25% (Tables 1, 2).

Širvintos district. Comparing the immunological indices of light smokers (n = 64) in Širvintos dis-

Table 1. **Leukocytes and indices of leukograms in the study subjects with reference to place of residence and smoking intensity**

District	Groups	n	Leukocytes	Lymphocytes		Monocytes		Neutrophils	
			$n \cdot 10^9/l$	%	$n \cdot 10^9/l$	%	$n \cdot 10^9/l$	%	$n \cdot 10^9/l$
Trakai	1	167	*5.3 ± 0.11**	31 ± 0.6**	1.6 ± 0.04*	*7 ± 0.2	0.3 ± 0.01*	60 ± 0.6**	*3.2 ± 0.06
	2	67	*6.3 ± 0.22**	32 ± 1.2	2.0 ± 0.11*	*6 ± 0.4**	0.4 ± 0.03*	59 ± 1.3	*3.8 ± 0.16**
	3	42	5.8 ± 0.24**	34 ± 1.7**	1.9 ± 0.08*	7 ± 0.4**	0.4 ± 0.03*	57 ± 1.7**	3.4 ± 0.21**
	4	6	5.9 ± 0.61	36 ± 2.9	2.1 ± 0.29	5 ± 1.7	0.3 ± 0.15	57 ± 0.0	3.3 ± 0.0
Širvintos	1	180	5.6 ± 0.11**	34 ± 0.7**	1.8 ± 0.05	6 ± 0.2*	0.3 ± 0.01*	58 ± 0.8	3.3 ± 0.09
	2	64	5.7 ± 0.19	32 ± 1.0**	1.8 ± 0.07	7 ± 0.4*	0.4 ± 0.02*	57 ± 1.1	3.3 ± 0.15
	3	35	6.1 ± 0.28**	33 ± 1.4	1.9 ± 0.11	7 ± 0.5*	0.4 ± 0.03*	58 ± 1.5	3.6 ± 0.22
	4	1	6.1 ± 0.0	28 ± 0.0	1.7 ± 0.0	4 ± 0.0	0.2 ± 0.0	61 ± 0.0	3.7 ± 0.0

1 – non-smokers, 2 – light smokers (1–10 cig. / 24 h); 3 – moderate smokers (11–20 cig. / 24 hs); 4 – heavy smokers (more than 20 cig. /24 h);
* – $p \leq 0.05$, ** – $0.05 < p \leq 0.1$.

Table 2. **T. B and NK lymphocyte populations in the study subjects with reference to place of residence and smoking intesity**

Disrtict	Groups	n	CD5		CD4		CD8		CD4/CD8	B (CD72)		NK (CD16)	
			%	n·10⁹/l	%	n·10⁹/l	%	n·10⁹/l		%	n·10⁹/l	%	n·10⁹/l
Trakai	1	152	61 ± 0.6*	1.0 ± 0.03*	41 ± 0.7	*0.7 ± 0.02	30 ± 0.6	0.5 ± 0.02*	1.5 ± 0.04	*10 ± 0.5**	0.2 ± 0.01	*21 ± 0.6	0.3 ± 0.02*
	2	59	61 ± 1.1*	1.2 ± 0.07*	42 ± 0.9	*0.9 ± 0.05**	29 ± 1.2	0.6 ± 0.05*	1.6 ± 0.07	*12 ± 0.9	0.2 ± 0.03	21 ± 1.2**	0.4 ± 0.03*
	3	40	66 ± 1.1*	1.2 ± 0.06*	42 ± 1.4	*0.8 ± 0.04**	31 ± 1.2	0.6 ± 0.04*	1.5 ± 0.11	12 ± 1.0**	0.2 ± 0.02	*18 ± 1.0**	0.3 ± 0.02*
	4	5	60 ± 4.8	1.3 ± 0.25	43 ± 2.7	0.9 ± 0.18	27 ± 2.7	0.5 ± 0.06	1.6 ± 0.17	7 ± 0.4	0.1 ± 0.02	30 ± 2.6	0.6 ± 0.12
Širvintos	1	162	61 ± 0.6	1.1 ± 0.03	41 ± 0.6	0.8 ± 0.02*	30 ± 0.6	0.6 ± 0.02	1.4 ± 0.04	11 ± 0.4	0.2 ± 0.01	18 ± 0.5**	0.3 ± 0.01*
	2	59	60 ± 1.0	1.1 ± 0.05	40 ± 1.0	0.7 ± 0.03*	31 ± 1.0	0.6 ± 0.03	1.4 ± 0.06	10 ± 0.6	0.2 ± 0.01	20 ± 1.0**	0.4 ± 0.02*
	3	30	62 ± 1.4	1.2 ± 0.08	40 ± 1.4	0.8 ± 0.05	31 ± 1.5	0.6 ± 0.05	1.3 ± 0.09	11 ± 1.1	0.2 ± 0.03	20 ± 1.2**	0.4 ± 0.03*
	4	1	52 ± 0.0	0.9 ± 0.0	38 ± 0.0	0.6 ± 0.0	18 ± 0.0	0.3 ± 0.0	2.1 ± 0.0	10 ± 0.0	0.2 ± 0.0	8 ± 0.0	0.1 ± 0.0

1 – non-smokers, 2 – light smokers (1–10 cig. / 24 h); 3 – moderate smokers (11–20 cig. / 24 h); 4 – heavy smokers (more than 20 cig. / 24 h);
* $p \leq 0.05$, ** $0.05 < p \leq 0.1$.

Table 3. **Blasttransformation, phagocytic activity of neutrophils, leukocyte migration inhibition reaction and concentration of immunoglobulins in the study subjects with reference to place of residence and smoking intensity**

District	Groups	n	Blasts	n	PhN	PhI	n	MI (%)			n	Ig (g/l)		
			(%)		(%)			25% ECA	50% ECA	75% ECA		IgG	IgA	IgM
Trakai	1	154	73 ± 0.7	157	98 ± 0.2*	6.1 ± 0.13	152	123 ± 5.0	63 ± 2.5	24 ± 1.3	165	10.5 ± 0.23	*1.9 ± 0.07	1.2 ± 0.04
	2	64	73 ± 1.1	62	96 ± 1.0*	5.8 ± 0.25	59	122 ± 7.1	64 ± 4.3	30 ± 3.0	66	10.2 ± 0.30	2.1 ± 0.10	1.3 ± 0.06
	3	41	73 ± 1.2	42	97 ± 0.4*	5.8 ± 0.24	38	120 ± 9.4	65 ± 5.9	26 ± 3.7	40	10.7 ± 0.54	2.1 ± 0.14*	1.2 ± 0.07
	4	6	77 ± 2.7	6	97 ± 1.0	5.4 ± 1.00	6	130 ± 17.4	67 ± 10.1	–	6	8.3 ± 1.10	1.8 ± 0.39	1.0 ± 0.14
Širvintos	1	168	72 ± 0.6	174	97 ± 0.3	*5.7 ± 0.13**	156	106 ± 3.9**	53 ± 2.2	25 ± 1.4	173	10.4 ± 0.19	*1.7 ± 0.05	**1.1 ± 0.03*
	2	60	73 ± 0.9	64	97 ± 0.3	*6.1 ± 0.23	56	123 ± 8.6**	56 ± 3.6	26 ± 2.0	59	10.3 ± 0.38	*1.9 ± 0.08	**1.0 ± 0.05
	3	34	73 ± 1.6	34	96 ± 1.3	6.4 ± 0.37**	34	117 ± 9.2	55 ± 3.0	23 ± 2.2	35	10.3 ± 0.45	1.8 ± 0.17	1.0 ± 0.04*
	4	1	71 ± 0.0	1	96 ± 0.0	4.2 ± 0.0	1	75 ± 0.0	26 ± 0.0	–	1	10.0 ± 0.0	1.3 ± 0.0	0.7 ± 0.0

1 – non-smokers; 2 – light smokers (1–10 cig. / 24 h); 3 – moderate smokers (11–20 cig. / 24 h); 4 – heavy smokers (more than 20 cig. / 24 h);
* $p \leq 0.05$, ** $0.05 < p \leq 0.1$.

trict with the indices of non-smokers (n = 180) of the same district, in the first group reliably higher was the percentage of monocytes (by 17%), the absolute quantity – by 33%, the percentage of CD16 index – 11%, the absolute quantity – 33%, IgA concentration in the blood serum – 12%, PhI – 7%. The LMIR index at a 25% ECA concentration was higher by 16%, *i.e.* the leukocyte sensibilisation was lower. The percentage of lymphocytes was lower by 6%, the absolute CD4 quantity – by 12% and IgM concentration in the blood serum – by 9% (Tables 1–3).

Comparing the same indices of moderate smokers (n = 35) in Širvintos district with the indices of non-smokers (n = 180), the total number of leukocytes in smokers was higher by 9%, the percentage of monocytes by 17%, their absolute quantity by 33%, the percentage of CD16 – 11%, absolute quantity – 33%, and PhI by 12%. The IgM concentration in the of blood serum was reliably lower (by 9%) (Tables 1–3).

Comparing same indices of moderate and light smokers, no difference in the immunological indices was detected.

Thus, it can be stated that the immune system of both light and moderate smoker groups, in comparison with non-smokers was stimulated. The stimulation of immunological indices was stronger in the inhabitants of Trakai district. Besides, the functions of the immune system of those (in Trakai district) who smoked 11–20 cig. / 24 h, in comparison with those consuming of 1–10 cig. / 24 h were suppressed. The above differences in Širvintos district were not identified.

SUMMARY

The activity of the immune system of the organism depended on the number of cigarettes smoked per 24 hours. With respect to the intensity of smoking, phenomena of suppression and stimulation, as well as compensation prevailed in all groups under investigation. The place of immunological indices in the scale of the above phenomena were not always of the same significance. Practically there were no groups with differentiation of exclusively suppressive or stimulative reactions, with respect to the place of residence and number of cigarettes smoked per 24 hours. Usually these went together. They were better differentiated in the groups with respect to the number of cigarettes smoked per 24 hours.

The suppressive impact of chemical matters confained in tobacco smoke on the immune system of humans was also identified in other terms, *i.e.* by analysing the data with respect to the number of cigarettes smoked per 24 hours. When comparing the immunological indices of smokers consuming 11–20 and 1–10 cig. / 24 h, the following indices were found suppressed in the contaminated Trakai district group: leukocytes (8%), neutrophils (11%), CD4 (11%), CD16 (14% and 25%). No suppression was observed in the slightly contaminated Širvintos district.

From the obtained results it can be summarised that both intensive smoking and long-term residence in an area contaminated with industrial siftings have a suppressive impact on the immune system of humans.

CONCLUSIONS

1. The immune functions of smokers of Trakai and Širvintos districts are stimulated, in comparison to the immune functions of non-smokers within the same districts.

2. The immune state of smokers in both Trakai and Širvintos districts depends on the number of cigarettes smoked per 24 hours, as well as on the place of residence.

3. The immunosupressive impact of chemical matters contained in tobacco smoke was determined by comparing the immunological indices of those who smoke 11–20 and 1–10 cig. / 24 h in the contaminated Trakai district (leukocytes, neutrophils, CD4 and CD16 were lower). No such differences were found in the matched groups of the slightly contaminated Širvintos district.

References

1. Orleans CT. Preventing tobacco-caused cancer: a call to action. Environ Health Perspect 1995; 103 Suppl 8: 149–52.
2. Capuano V, Lamaida N, De Martino M et al. Association between white blood cell count and risk factors of coronary astery disease. G Ital Cardiol 1995; 25 (9): 1145–52.
3. Boyle P, Moisonneuve P. Lung cancer and tobacco smoking. Lung Cancer 1995; 12 (3): 167–81.
4. Ginns LC, Hoyos AD, Brown MC et al. Elevated concentration of Soluble Interleukin-2 receptors in serum of smokers and patiens with lung cancer. Am Rev Respir Dis 1990; 142: 398 –402.
5. Li Q, Geiselhart L, Mittler JN et al. Inhibiton of human T lymphoblast proliferation by hydroquinone. Toxicol Appl Pharmacol 1996; 139 (2): 317–23.
6. Kazbarienė B, Kemeklienė R, Krikštaponienė A et al. The immune state of humans with respect to tobacco smoking. Part 1. Acta Medica Lituanica 2000; 7 (1): 41–4.
7. Kazbarienė B, Kemeklienė R, Krikštaponienė A et al. The immune state of humans with respect to tobacco smoking. Part 2. Acta Medica Lituanica 2000; 7 (3): 110–4.

8. Критерии иммунологического дисбаланса как возможные факторы онкологического риска. Под ред. Монцевичюте-Эрингене Е. В. Вильнюс. Мокслас, 1986.

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GYVENTOJŲ IMUNINĖS BŪKLĖS PRIKLAUSOMYBĖ NUO TABAKO RŪKYMO. 3 DALIS

S a n t r a u k a

Į veikiančius organizmą įvairius veiksnius imuninė sistema atsako nuolat kintančia funkcija – besiformuojančiomis supresinėmis ir stimuliacinėmis reakcijomis. Mūsų ankstesni darbai parodė, kad viena iš imuninės sistemos funkcijos sutrikimo priežasčių – aplinkos teršimas. Todėl šio darbo tikslas buvo tirti pramoninėmis išlakomis užteršto rajono (Trakai, n = 282) ir jomis silpniau užteršto rajono (Širvintos, n = 282) gyventojų imuninės homeostazės sutrikimus priklausomai nuo tabako rūkymo intensyvumo. Pagal rūkymo intensyvumą tiriamieji buvo suskirstyti į 4 grupes: I – nerūkantieji, II – silpnai rūkantys (1–10 cigarečių/24 val); III – vidutiniškai rūkantys (11–20 cigarečių/24 val.); IV – daug rūkantys (daugiau 20 cigarečių/24 val.). Nustatyta, kad organizmo imuninės sistemos funkcijai turėjo įtaką užterštoje pramoninėmis išlakomis aplinkoje gyvenančių žmonių surūkytų cigarečių skaičius per parą. Tabako dūmų cheminių medžiagų imunosupresinis poveikis yra nustatytas lyginant užteršto pramoninėmis išlakomis Trakų rajono rūkančiųjų po 11–20 ir po 1–10 cigarečių per parą imunologinius rodiklius (pirmųjų buvo mažesni leukocitai, neutrofilai, CD4, CD16). Tuo tarpu silpniau užteršto pramoninėmis išlakomis Širvintų rajono tokiose pačiose grupėse skirtumų nerasta.