

ALTERATIONS IN HUMAN LYMPHOCYTES CYTOGENETIC PARAMETERS AFTER INDIRECT CONTACTS WITH AGENT ORANGE ON THE CONTAMINATED TERRITORIES

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An Agent Orange (AO) ecocyclic activity in the South Vietnam is studied for more than 20 years. The entire conditions developed on the sprayed area provided the formation of the complex specific factor. The main ecotoxicological components of this environmental factor are the residuals of dioxin. In studying of the environmental factors' influence on the population's health the dioxin-containing ecotoxic factor (DEF) should be considered as the self-acting. The leading role of living on the sprayed territory in the worsening of health status of this region population has been shown during the analysis of influence of several risk factors (nutrition, contacts with pesticides, smoking and alcohol consumption, diseases, etc.) on the medically significant manifestations of past contacts with AO consequences [1,2].

The cytogenetic study of cultured lymphocytes [3] was carried out in the limits of general epidemiological and clinical laboratory study of the population in Song Be Province and Thu Dau Mot town's area (South Vietnam). The patients were seldomly selected among the statistically categorized exposure risk groups (ERG) with different level of past potential exposure to AO [4]. Controls (n=10) were selected in Chanh My and Tuan An villages, two groups of patients were from Binh My village - BMD (n=16), with direct contacts with AO in the past; and BMI (n=17), with indirect AO contacts, just residents of the sprayed territory, i.e., exposed to DEF. The general methods used and the characteristics of the parameters analyzed were given earlier [3,5]. This paper presents the results of the AO indirect influence analysis, and of the DEF particular activity in the observed alterations in the cytogenetic status of cells. The relations of these shifts with the other changes in lymphocytes' characteristics and in immune status are shown as well.

Considering the role of such factor as residence on the sprayed territory we delineated the following groups: natives, living more than 10 years, and living less than 10 years in the

conditions of chronic contacts with DEF. Unfortunately it was impossible to escape the influence of the most prominent and even confounding factor as smoking. This factor is obviously obligator for male population in Vietnam.

The results obtained are presented in the Table 1. The mostly influenced by the exogenous factors and by DEF first of all were persons settled in Binh My village more than 10 years ago. The highest values of the cytogenetic parameters were registered in their cells. This was characteristic for those with AO direct contacts in the past, and for those who suffer only DEF influence. The degree of the latter effect is even higher. The greatest percentages of cells with high SCE numbers (HFC) were observed in these patients particularly - up to 42.5%, and 30% as the modal values; as compared to 2.5% in the controls. The rate of environmentally determined SCE (eSCE) varied in the range of 37-62% in people from the BMI group with more than 10 years of residence. The people from the BMD group with the same living period had eSCE values in the range of 12-56%. The control group patients (where the majority were smokers) had no more than 39%.

We tried to explain these differences from the following point of view - as the exhaustion of the cells' reserve potentials (CRP) for reparation and replication. The cells are just eliminated from blood circulation when their inner reparative systems unable to restore the primary and successive lesions. So, these cells either fail to enter the replicative cycle and thus can't be registered by the routine cytogenetic techniques, or die, and are processed by the phagocytic cells increasing the level of peroxides in the blood plasma. The cells' decreased ability to use their CRP is proved by the fact of lower SCE levels induced by additional mutagenic loading of the cultures from persons inhabiting the sprayed area. In our study it was mitomycin C (0.1 mcg/ml) that produced almost 4 times increase in eSCE in the control group and only 2.5 times increase in eSCE of the Binh My patients [6].

Besides, the indirect evidence for our postulate can be seen in the fact of T-lymphocytes proportion decrease in the peripheral blood of Binh My villagers apart from the later settlers. While the average T-cells levels were rather close to those seen in the controls, the acute decrease in the modal levels can be observed - as for T-cells percentage, and for T-helpers as well (Table 1). In those living in the sprayed area for <10 years all the parameters mentioned above are altered also, but to a lesser extent. At the same time these people have very high indices of phagocytic activity. It may reflect the organism primary reaction on the enhancement of destructive processes in the tissues of these people. In spite of the fact that the majority of registered effects represent tendencies only, we believe them to be the primary indicators of greater shifts probably able to be really manifested while examining significant samples.

Thus, the biochemical shifts [7] and the immunodepressive states [5,8] in the people suffering DEF influence are supported by the level of the cytogenetic changes. This can be considered as the evidence for the alterations in mechanisms of cell proliferation and differentiation. This fact may serve as one of the basic statements that the observed sub clinical alterations will be able in the future to proceed as medically significant - while progressing of the processes of morphogenesis, teratogenesis and/or carcinogenesis.

Table 1. Cytogenetic and Immunologic characteristics of patients with different longevity of contacts with Dioxin-containing Ecotoxic Factor (DEF) in Song Be Province (South Vietnam).

ERG	DEF	Number of patients (years)		sSCE	gSCE	eSCE	eSCE Rate %	HFC N	HFC %	T-cells %	T-helpers %	T-suppressors %	PHAG	SIC	SICTER	IGA	IGM	IGG
CON	0	10	Average	5.95	4.69	1.26	20.81	2.60	6.50	57.00	41.80	17.50	58.20	169.4	23.1	1.86	2.46	16.37
TROL	<10	9 sm+	Range	4.16-7.75	3.28-6.03	0.36-2.1	7.02-39.03	0-8	0-20	38-84	20-68	2.0-41.0	32-80	134.4-300.0	7.4-64.4	0.9-2.36	0.8-4.36	9.0-24.32
		1 sm-	Mode	5.70	4.20	1.05	19.06	1.00	2.50	52.00	40.00	16.00	44.00	150.0	18.3	1.70	2.18	12.40
		[800]	St.Er.	0.37	0.31	0.20	3.06	0.95	2.36	4.48	4.77	3.71	4.93	15.8	5.1	0.17	0.36	1.91
	<10	7	Average	7.64	4.79	2.85	37.18	6.29	15.71	70.86	51.71	20.57	80.00	130.2	15.1	2.08	1.65	12.87
		5 sm+	Range	5.35-8.60	3.53-6.25	1.82-4.45	23.59-53.74	1.00-10.00	2.50-25.00	52-78	46.0-60.0	6.0-30.0	46-90	37.7-214.8	8.0-26.3	0.50-3.58	1.00-2.30	8.00-20.32
		2 sm-	Mode	7.75	4.03	2.45	34.02	5	12.50	78.00	52.00	20.00	90.00	126.5	10.1	1.92	1.35	10.24
BMI	>10	[540]	St.Er.	0.42	0.39	0.35	3.74	1.19	2.97	3.40	1.71	2.89	5.86	20.2	2.9	0.37	0.19	1.84
		6	Average	8.3	4.29	4	47.76	10.67	26.67	57.33	46.67	14.00	62.67	120.8	10.3	2.19	1.72	16.69
		5 sm+	Range	6.33-9.48	3.33-5.63	2.75-5.88	36.95-62.03	3.00-17.00	7.50-42.50	28-80	12.0-76.0	4.0-24.0	48-80	98.2-160.0	0.8-16.4	1.63-2.60	1.20-2.49	10.24-29.44
	>10	1 sm-	Mode	9.48	3.6	3	41.98	12	30.00	32.00	36.00	20.00	52.00	105.7	6.4	1.85	1.43	14.08
		[480]	St.Er.	0.59	0.36	0.5	3.52	2.26	5.65	8.92	9.10	3.54	5.33	9.6	2.4	0.16	0.19	2.69
		4	Average	5.72	3.47	2.26	39.47	2.50	6.25	54.50	44.50	10.00	56.00	68.5	7.5	2.63	1.74	13.60
Natives	>10	3 sm+	Range	4.56-6.65	2.84-4.58	1.56-2.20	31.13-46.62	0.00-5.00	0.00-12.50	40-76	32.0-70.0	4.0-20.0	24-88	30.9-98.2	0.4-18.6	1.85-3.19	1.39-2.24	9.92-18.24
		1 sm-	Mode	4.56	2.84	1.56	31.13	0.00	0.00	40.00	32.00	4.00	56.00	30.9	0.4	1.85	1.39	9.92
		[160]	St.Er.	0.48	0.39	0.29	3.98	1.19	2.98	7.63	8.66	3.56	13.06	15.7	4.0	0.29	0.18	1.80
Total	>10	17	Average	7.42	4.30	3.12	41.45	6.94	17.35	62.24	48.24	15.76	68.24	112.4	11.6	2.25	1.70	14.39
		13 sm+	Range	4.56-9.48	2.84-6.25	1.56-5.88	23.59-62.03	0-17	0-42.5	28-80	12-76	4.0-30.0	24-90	30.9-214.8	0.4-26.3	0.5-3.58	1.0-2.49	8.00-29.44
		4 sm-	Mode	9.48	3.83	2.75	41.51	5.00	12.50	72.00	48.00	20.00	56.00	98.2	10.1	1.85	1.62	10.24
BMD	<10	[1180]	St.Er.	0.37	0.25	0.28	2.37	1.20	3.01	4.06	3.67	2.09	4.73	11.0	1.8	0.18	0.10	1.28
		6	Average	6.96	4.57	2.42	32.94	4.00	10.00	53.67	34.00	19.67	56.33	134.6	25.4	2.01	1.62	20.56
		2 sm+	Range	5.80-9.23	4.00-5.03	0.73-5.20	12.59-56.34	1.00-10.00	2.50-25.00	28-84	12.0-76.0	8.0-32.0	20-86	91.4-207.1	10.4-41.3	1.32-2.58	1.08-2.57	14.72-25.60
	<10	4 sm-	Mode	6.45	4.03	1.85	27.82	4.00	10.00	32.00	20.00	12.00	24.00	103.0	13.1	1.40	1.10	15.04
		[480]	St.Er.	0.49	0.19	0.61	5.85	1.29	3.23	8.68	9.28	3.81	11.99	16.7	5.0	0.23	0.23	2.14
		10	Average	5.79	4.45	1.34	23.09	2.10	5.40	62.10	42.44	19.90	52.60	163.2	16.0	2.36	1.68	21.17
Natives	>10	7 sm+	Range	4.68-7.63	3.32-5.63	0.57-2.00	10.00-31.97	0.00-8.00	0.00-20.00	40-84	12.0-72.0	6.0-44.0	2.0-90.0	77.4-358.4	1.9-44.9	1.34-4.20	0.41-2.59	10.56-32.64
		3 sm-	Mode	5.20	4.08	1.10	21.37	1.00	0.00	52.00	44.00	24.00	36.00	114.0	11.1	1.84	1.39	19.20
		[800]	St.Er.	0.32	0.25	0.15	2.26	0.86	2.14	4.80	6.48	4.11	8.52	30.9	3.7	0.28	0.19	1.95
Total	>10	16	Average	6.23	4.50	1.74	26.78	2.81	7.13	58.94	39.07	19.81	54.00	152.5	19.5	2.23	1.66	20.94
		9 sm+	Range	4.68-9.23	3.32-5.63	0.57-5.20	10.0-56.34	0-10	0-25	28-84	12-76	6.0-44.0	12.90.0	77.4-358.4	1.9-44.9	1.32-4.2	0.41-2.59	10.56-32.64
		7 sm-	Mode	5.80	4.80	1.55	25.93	1.00	0.00	56.00	28.00	8.00	50.00	116.0	13.1	2.38	1.34	25.44
	>10	[1280]	St.Er.	0.30	0.17	0.27	2.78	0.74	1.83	4.38	5.28	2.86	6.74	20.1	3.1	0.20	0.14	1.42

ERG - Exposure Risk Groups; BMI - Binh My villagers with Agent Orange indirect contacts; BMD - Binh My villagers with Agent Orange direct contacts; * - number of cells per cytogenetic analysis; gSCE - spontaneous Sister Chromatid exchanges; gSCE - genetically determined SCE; eSCE - environmentally determined SCE; HFC - cells with SCE high frequencies; PHAG - phagocytic index; SIC - serum circulating immunocomplexes; SICTER - testostable SIC; IGA, IGM, IGG - immunoglobulins levels (g/l).

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