Consistent Deterioration of General Health Status in South and North Vietnamese Exposed to Agent Orange

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Introduction: A series of specialized integrated epidemiological and clinical laboratory investigations carried out in the Joint Vietnam-Russian Tropical Center in 1988 - 1993 gave evidences of the reality and medical significance of the long-term health consequences of past direct contacts with Agent Orange (AO) in rural South Vietnamese. Significant associations between the questionnaire-derived statistically grounded measures of past direct exposure to AO (early toxic responses, Medical Equivalents of Toxodose, "MET1,2"; Exposure Risk Groups, "ERG") and certain characteristics of current general health status in apparently healthy persons (symptoms and signs of sub clinical pathological conditions for different systems of the organism; Index of Poor Health Status); specific patterns of pathological manifestations associated with separate influence of main health risk factors; the reality of exposure-response-like relations between ERG-based estimates of the exposure and values of the Index of Poor Health Status (Effect Development Risk Groups), and increased susceptibility of exposed persons to infectious pulmonary diseases during epidemic period[1,2] have been found with the internal and external comparisons. These epidemiological findings indicated a practicability of the employed approach and supported a hypothesis of causal relationships between the exposure and current health outcomes that enabled to assess Attributable Risk Fractions for main health risk factors in the sub clinical state (Fig. 1).

Objective: The objective of present study was to investigate a consistency (reproducibility) of established associations in another contingent of exposed rural Vietnamese to verify a reliability of the employed methodology and hypothesized causality.

Methods: A community-based cross-sectional epidemiological study in the sub clinical state has been performed in the village Bac Hong (Dong Anh, Hanoi, 1993) by the same way as in the villages Chanh My and Binh My (Song Be, 1989)[1]. A contingent under the study consisted of peasants living in Bac Hong after the wartime (m, 40-60; rice farming) with similar socio-economic status and life style, adequate nutrition, relatively low pesticides usage and alcohol consumption. The persons with a history of direct contacts with defoliants (1 - 5 times) during a military service in the South Vietnam that have been accompanied by pronounced symptoms and signs of primary toxic responses and were in accordance with US HERBS Tape data are categorized as "exposed". In a situation of several direct exposures, characteristics of primary toxic responses have been recorded for the most severe case to assess MET1 and MET2 values. "Unexposed" part of the

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Fig.1. Attributable risk fractions for the main health risk factors in a contingent of apparently healthy rural South Vietnamese (1989)

(Nutrition: < 100 g meat/week; S - smoking: > 10 cigarettes/d;
M - past malarial diseases: > 5 y after the last case)

Exposure risk groups

Health Risk Factors	AO	DEF	Nutrition	S	M ± S
Comparison groups [x] :	BM III /	BM II + /	BM II + /	BM II + /	BM II + /
+/− risk factor influence	BM II	BM II −	BM II −	BM II −	BM II −
N (m, 31-50)	70 / 121	142 / 43	150 / 93	64 / 121	29 / 168

Symptoms and signs

148 Tachycardia	**.459***	-.191	-.068	-.132	.025
172 Vomiting	**.581***	.082	.109	-.014	.155
175 Constipation	**.514***	-.292	.039	-.133	-.057
143 Dyspnea, exertion	**.288***	.023	-.034	-.076	-.017
137 Pain-chest	**.188***	.068	-.051	-.045	.002
191 Spots before the eyes	**.350***	**.816***	-.113	**.493***	**.472***
158 Pain-legs, rest	**.319***	-.049	-.028	-.352	.025
169 Thirst, permanent	**.229***	.058	-.113	-.151	-.009
131 Cough, total	.150	-.043	-.031	-.284	-.036
157 Pain-legs, walk	**.296***	-.049	-.113	-.141	-.057
150 Pain-heart	**.202***	-.020	-.031	-.237	-.016
185 Blurred vision	.184	**.388***	-.028	-.058	.094
155 Pain-loins	.064	.218	-.066	-.189	-.041
163 Weight loss	.176	.058	-.060	-.399	-.006
196 Frequent URD	.173	-.135	-.023	-.315	-.026
141 Headache, frequent	.162	**.388***	-.113	**.447***	.049
133 Cough, at night	.165	.082	-.113	-.318	-.057
170 Thirst, frequent	.112	.082	-.113	-.268	.119
192 Impaired dark adapt.	-.088	**.541***	**.555***	**.865***	**.296***

[x] - Free from persons with high alcohol consumption and frequent contacts with pesticides. * - p<0.05.

contingent included war veterans and peasants who had never been in direct or indirect contacts with war phytotoxicants. New index of general health status ("IGHS", person-years of well-being life) accounting adaptability of the organism has been introduced basing on the procedure of Kaplan (1989) [4] to evaluate alterations in the subjective health associated with an influence of main health risk factors in contingents of South and North Vietnamese.

Results: The results confirming a leading role of past direct contacts with AO in significant deterioration of current general health status expressed in terms of IGHS and comparable contribution of past malarial diseases ("M", > 10 y after the last case) to this effect (particularly in exposed veterans) in both contingents free from persons with high alcohol consumption and frequent contacts with pesticides are presented in the following table.

SOUTH (Binh My, m, 31-50, 1989)					NORTH (Bac Hong, m, 40-60, 1993)				
N	406	61	84	22	N	128	80	14	62
IGHS*	.798	.787	.611	.537	IGHS*	.687	.610	.561	.562
AO / M	$-$ / $-$	$-$ / $+$	$+$ / $-$	$+$ / $+$	AO / M	$-$ / $-$	$-$ / $+$	$+$ / $-$	$+$ / $+$
$-$ / $-$	--	x	xx	xx	$-$ / $-$	--	xx	xx	xx
$-$ / $+$	--	--	ns	x	$-$ / $+$	--	--	ns	x
$+$ / $-$	--	--	--	x	$+$ / $-$	--	--	--	ns
N	243	224	74	32	N	120	88	37	39
IGHS*	.766	.780	.620	.541	IGHS*	.669	.642	.563	.562
AO / S$^+$	$-$ / $-$	$-$ / $+$	$+$ / $-$	$+$ / $+$	AO / S$^+$	$-$ / $-$	$-$ / $+$	$+$ / $-$	$+$ / $+$
$-$ / $-$	--	ns	xx	xx	$-$ / $-$	--	ns	xx	xx
$-$ / $+$	--	--	xx	xx	$-$ / $+$	--	--	x	x
$+$ / $-$	--	--	--	ns	$+$ / $-$	--	--	--	ns

* – "Multifactor ANOVA", Averages. $^+$ – Smoking, > 10 cigarettes / day.
X, XX – $P < 0.05$, $P < 0.001$ ("Mann-Whitney Rank Test").

There were no significant differences between IGHS values in sub groups of exposed North Vietnamese stratified by the number of direct contacts (1-2 / >2; not shown). At the same time, similar associations between the questionnaire-derived characteristics of primary toxic responses to AO as well as the exposure-response-like relations between ERG-based measures of exposure intensity and characteristics of sub clinical deterioration of current health status have been found in both contingents using MET1,2 values (Fig. 2). Different resolution power of these approaches to semi-quantitative

Fig. 2. Consistent primary toxic (MET1,2) and long-term sub clinical (IGHS) responses to the direct contacts with AO in contingents of South (m, 31-50) and North (m, 40-60) Vietnamese

Contingents:	SOUTH (Chanh My, Binh My, Song Be, 1989)	NORTH (Bac Hong, Dong Anh, Hanoi, 1993)

Associations between MET 1 and MET 2 values

N (MET1 and MET2 ≠ 0)	107	76
Linear Regression Model	MET2 = 0.829 x MET1 + 0.157	MET2 = 0.753 x MET1 + 0.195
Correlation Coefficient	0.690	0.732

Deterioration of general health status in statistically defined Exposure Risk Groups

ERG:	CM1	BM2	BM3 *	BM4 *	p ^{X}	BH1	BH2 **	BH3 **	p ^{X}
AO	no	no	yes	yes		no	yes	yes	
DEF	no	yes	yes	yes		no	yes	yes	
N	276	190	74	33		208	44	32	
MET1	–	–	.06 - .53	.53 -.82		–	< .53	≥ .53	
MET2	–	–	.10 - .70	.50 -.90		–	aver.=.42	aver.=.72	
IGHS$^+$	.806 - .852 **.829** 345.7	.717 - .774 **.746** 264.7	.598 - .689 **.644** 194.7	.454 - .589 **.522** 130.6	**0**	.637 - .678 **.657** 160.0	.560 - .649 **.604** 130.2	.450 - .555 **.503** 71.8	**<10^{-6}**

*, ** - "Cluster Analysis" (MET1 / MET2), "Statistical Grouping" (MET1). $^+$ - **Index of General Health Status**; subjective health: **1 → 0** - deterioration: 95% C.I., Averages, Average Ranks.

^{X} - "Multifactor ANOVA" for **IGHS** with the factors: **"ERG"**, **"M"** - history of malarial diseases (>10 y after the last case), **"S"** - smoking (> 10 cigarettes/d), **alcohol consumption** (> 0.5 l / m), **pesticides** > 10 contacts / y). **Main effects:** South - **"ERG"**, **"S"**; North - **"ERG"**, **"M"**. **2-Factor Interactions** - **"No"** in both contingents.

assessment of past direct exposure allows to presume better informativity of MET1,2 values as integrated characteristics of the exposure intensity, at least partly reflecting individual differences in susceptibility to primary toxic and subsequent health effects of dioxin-containing chemicals.

Sufficient qualitative similarity between specific patterns of sub clinical pathological manifestations associated with a history of exposure to AO that is registered even on the background of health consequences of past malarial disease in veteran's contingent (p<0.05, "Spearman Rank Correlations") and the absence of similarity between the patterns calculated for health consequences of AO and past malarial disease have been found in both contingents (Fig. 3).

Fig. 3. Specific patterns of sub clinical pathological manifestations associated with the histories of exposure to AO and malarial disease in contingents of South and North Vietnamese.

(M–H OR, Epi Info 5.01; *- 95% C.I. excludes 1.0; +-Chi square test, p <0.05)

Health risk factors	AO (-M,-S)	M (-AO,±S)	AO+M (±S)	M (-AO,±S)
Contingents	SOUTH	SOUTH	NORTH	NORTH
Comparison sub groups	BM3+4/BM2	BM2 + / −	BH2+3/BH1	BH1 + / −
N	70 / 121	29 / 168	60 / 91	79 / 115
148 Tachycardia	6.22*	1.58	2.64*	1.41
172 Vomiting	5.95*	2.43*	2.52*	1.07
175 Constipation	5.77*	4.38*	1.58*	1.96+
143 Dyspnea, exertion	3.29*	2.41*	2.50*	1.14
137 Pain-chest	2.76*	4.45*	1.85+	1.91+
191 Spots before the eyes	2.68*	4.55*	2.44*	0.81
158 Pain-legs, rest	2.62*	0.62	1.25	2.63+
168 Increased appetite	2.62*	0.99	1.53	0.97
169 Thirst, permanent	2.38*	3.96*	1.35	2.07*
131 Cough, total	2.24*	1.10	1.33	0.75
157 Pain-legs, walk	2.24*	0.91	1.43	2.08*
150 Pain-heart	2.19*	1.36	2.14*	2.64*
185 Blurred vision	2.14*	2.44*	1.25	1.93*
155 Pain-loins	1.93+	2.90*	2.15*	1.19
163 Weight loss	1.92+	2.27	1.81	1.42
196 Frequent URD	1.86+	1.03	2.17*	1.31
141 Headache, frequent	1.70	3.39*	1.31	1.04
133 Cough, at night	1.64	2.11	1.94	.65
170 Thirst, frequent	1.36	1.80	0.54	1.54
161 Pain-joints	1.10	1.61	1.94	1.27
180 Anal bleeding	1.05	1.80	2.24	1.30
192 Impaired dark adapt.	0.74	8.35*	2.94*	1.62
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"±S"- Smokers and non smokers; no differences in smoking habitat between the comparison sub groups (chi square test, p>0.05).

Conclusions: Significant similarity in the associations between questionnaire-derived characteristics of primary toxic responses to past direct contacts with AO (MET1, MET2) and between a history of exposure to AO or the ERG-based measures of the exposure and current sub clinical health outcomes, the reality of exposure-response-like relations between ERG-based exposure estimates and subjective health status (IGHS) as well as sufficient similarity between specific patterns of sub clinical pathological manifestations associated with a history of direct contacts with AO found in two different contingents of rural South and North Vietnamese using one and the same technique confirmed sufficient reliability of the employed methodology, on the one hand, and indicated significant consistency of the observed effects, on the other hand. These results give one more evidence of the reality of significant subjective health outcomes associated with a history of direct contacts with AO in Vietnamese and represent a strong argument in favour of the exposure-response causality.

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