

Significant Associations Between Questionnaire - Derived Measures of Past Exposure to Agent Orange and Health Outcomes in Subpopulation of Rural S. Vietnamese.

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Dioxin's toxicokinetics and biological potency dependence on peculiarities of exposure, concomitant chemicals, certain biologically active endogenous and exogenous substances, and genetic and medico-biological features of the organism determine high uncertainty in estimating effective dose and probabilistic character of dioxin-related health outcomes formation and development. Presently, a practicable methodology for dioxin health risk assessment may be based on comparative investigation of clinically significant manifestations incidence in human groups ranged according to the likely extent of dioxin exposure and homogenous regarding influence of other toxicokinetically and pathogenetically significant factors.

The purpose of this study was to investigate associations between questionnaire-derived measures of past potential exposure to Agent Orange (AO) and characteristics of current health status (complaints) more than 20 years postexposure among peasants from the control village Chanh My "CM" (Thu Sau Mot) and AO-treated village Binh My "BM" (Tan Uyen)¹.

Statistical categorization of age- and sex- adjusted groups according to increasing extent of potential past exposure and influence of other place-specific factors has been performed taking into consideration self-reported symptomocomplexes of early toxic responses from the organs of contact and the organism for cases of potential direct contacts (Medical Equivalent of Toxodose 1,2 correspondingly) and history of residence for potential indirect exposure from the environment.¹

The following contingent (m/f; 31-50; similar conservative socio-economic and nutritional status in covillagers; statistically homogeneous regarding smoking, low use of conventional pesticides, low alcohol consumption, and malarial morbidity) and increasing exposure risk groups (ERG) were selected to illustrate design and initial results of the study for this communication:

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ERG:	CM 1	BM 2	BM 3	BM 4	BM 5	BM 6
MET 1*	0	0	0	≤.269 m/f	.269<<.507 m .269<<.567 f	≥.507 m ≥.567 f
MET 2*	0	0	0	.240 m .290 f	.420 m .360 f	.660 m .650 f
indir. ^x	-	-	+	+	+	+
T, y ^o	natives	≤10	>10	>10	>10	>10
m, N	346	54	158	50	43	18
f, N	381	95	209	50	45	33

* Exposure index selected for statistical differentiation of a contingent with potential direct contacts with AO (1965-1971) for initial evaluations. One-dimensional classification procedure realizing a concept of statistically "best" partition of an object into groups (4→6) with the dense allocation of values in case when the grouping principle is not specified otherwise has been employed. ("Statistical Grouping", Statex2, Moscow, 1992)

+ Corresponding MET2 median values.

^x Potential indirect exposure from the environment due to residing in the village during AO treatment (1967-1968) and/or subsequent 10 years.

^o Duration of residence in the village up to the beginning of epidemiological examination (1988-1989).

Complaints frequency association with increasing risk of exposure has been estimated in the defined ERG ("Contingency Table", Statgraphics v.3.0). The following groups of complaints were distinguished: 1 - complaints which are positively and significantly associated with the risk of exposure (D.F.=5; Chi-square, $p < 0.05$; Contingency coeff. "c.c.", $p < 0.05$; Conditional gamma " γ " > 0 , $p < 0.05$) in all sex/age-adjusted groups - 11 positions, 2 - complaints associated with the risk of exposure in certain sex/age-adjusted groups - 23, 3 - non associated positions - 4 (Data not shown). Then, "improved" indices of general health status (IHS) were calculated for each person: $IHS = C/N$, where C is a sum of exposure risk - associated complaints and N is a number of corresponding positions in a questionnaire for a human group under the study. Examples illustrating complaints frequency and IHS values associations with the increasing risk of exposure in the above described contingent are shown in the following tables:

ERG	Complaints frequency, %, rounded			
	Cough		Tachycardia	
	m	f	m	f
CM1	36.6	33.9	17.6	41.7
BM2	48.1	35.8	22.2	47.4
BM3	47.5*	41.6	27.2*	46.9
BM4	74.0 ⁺	54.0 ⁺⁺	56.0 ⁺	46.0
BM5	72.1	66.7	53.5	64.4 ⁺
BM6	66.7	67.6	66.7	88.2 ⁺
P_{χ^2}	3.3×10^{-8}	1.6×10^{-6}	3.1×10^{-13}	3.8×10^{-6}
c.c.	.246	.202	.302	.197
γ	.361	.274	.455	.214

*, ⁺ - The beginning of statistically significant ($0 < p < .03$) and increasing differences between the ERG "1", the ERG "2" and following ERG.

IHS, "Mann-Whitney Rank Test", (Statgraphics, v. 3.0)

m	1	2	3	4	5	6	f	1	2	3	4	5	6
1	##						1	##					
2	***	##					2	***	##				
3	***	ns	##				3	***	ns	##			
4	***	***	***	##			4	***	ns	ns	##		
5	***	***	***	ns	##		5	***	***	***	**	##	
6	***	***	***	*	ns	##	6	***	***	***	***	*	##

*, **, *** - $p < .05$, $p < .01$, $p < .001$

From these data a significant positive association of given pathological signs manifestation and general health status deterioration with increasing exposure risk is evident.

The analogous results were obtained for a number of complaints and indices of general health status in other contingents (not shown). At the same time, highly significant differences between IHS values in the ERG 1 and 2 and insignificant distinctions between the ERG 2 and 3 are indicative of a medical role of place-specific (CM or BM)

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factor and of a problem of adequate comparison groups selection. Nevertheless, significant differences in questionnaire-derived measures of health status between persons from the ERG 3→6 (equal values of T, which may serve as integrated characteristic of place-specific factors influence) bear evidences of long-term health consequences of past exposure to AO in this contingent at least for the cases of direct contact.

Further development of this approach (investigation of the relationships between different components of MET1,2 indices and complaints frequencies and IHS values) seems to be very promising for :

- 1- elaborating an adequate epidemiologically suitable past exposure estimation method for AO as well as for other similar cases of dioxin-containing chemicals impacts;
- 2 - selecting persons with significantly increased/decreased individual susceptibility;
- 3 - establishing specific symptomocomplexes of remote dioxin-related health outcomes;
- 4 - investigating medical significance of different pathways of dioxin-containing chemicals entry to organism.

As a whole, a realistic statistically "safe" level of dioxin exposure for each concrete situation may be specified by this approach for such human groups, where rates of medically significant manifestations do not exceed the values typical for each adequate dioxin-unexposed comparison group. Also, generally accepted criteria of health status normality for a group under the study, possibilities of increased individual susceptibility to dioxin in statistically insignificant number of persons in the ERG and remote health outcomes development must be taken into consideration to confirm this conclusion.

1 Roumak V., Poznyakov S., An N., Kim Chi N., Thu T., Sofronov G., Sokolov V., Kountzevitch A. Epidemiological and clinical laboratory studies on health consequences of Agent Orange in the South Vietnam. *Dioxin'* 92. 10:275-8.