

RISK (po)

Retrospective epidemiological data on reproductive events registered in South Vietnam villages

Natalia Oumnova*, Huynh Thi Kim Chi, Vladimir Roumak***

* Joint Vietnam-Russia Tropical Research Centre, Gia Thuy, Gia Lam, Hanoi;

** Song Be province MCH/Family Planning Centre

1. Introduction

The manifestations of reproduction pathology increase in families living in sprayed by Agent Orange (AO) Binh My village have been shown ¹⁾ during the epidemiological survey in the Song Be province (1988-1989, m/f, N=2235). The residents of Binh My village are considered to be at risk of ecotoxicological factors pressure with dioxin as the main component ^{2,3)}. After specialized analysis of the village, contingent exposure two large groups were revealed and characterized ²⁻⁴⁾. The following evaluation of health indices and different clinical and laboratory parameters was carried out according to these Exposure Risk Groups (ERG). The ERGs were represented: ERG III - by persons with past direct exposure to AO and current exposure to dioxin-containing ecotoxicological factor (DEF); ERG II - by persons settled on the sprayed territory after the war-time and currently exposed to DEF. The external referent group (ERG I) was studied in the close village Chanh My with no history of AO spraying.

The representatives of all three ERGs were examined during primary medical survey simultaneously with questionnaires' collection. The Index of General Health Status (IGHS) was estimated ²⁾ along with the analysis of the Long-Term Medical Consequences produced on the base of registered symptoms and signs grouped for systems and organs possibly affected by the exposure ^{3,5)}. The significant deterioration of health status in ERG III members was indicated by IGHS ²⁾. This paper considers the possible role of lower IGHS in the reproduction pathological events observed in villagers of the Song Be province.

2. Results

The profiles of the reproduction function pathology as subjected by questions in the epidemiological questionnaire and according to membership in different ERGs are shown in table 1. The assessment was based on the females' answers (N=1186), because the appraisals of abortions' and stillbirths' frequencies given by males were 4 to 10 times lower. There were no differences in appraising the congenital abnormalities. The persons (N=70) with past and current diagnosis of malaria were excluded from the analysis as well as those with inflammations that could be recalled as coinciding with pregnancy.

The reproductive events are age-dependent so the ERGs were stratified according to the following age groups: 20-30; 31-50; 51-60. The increase in cases of recurrent stillbirths in the ERG III eldest group can be explained mostly by aging processes.

RISK (po)

Table 1. Reproduction function pathology in Exposure Risk Groups (two South Vietnam villages, N=1186, aged 20-60). Non-parametric statistics, Chi-square

A. No stratification by age	I ^a	II ^b	III ^c	p ^{ab}	p ^{bc}	p ^{ac}
Number of families examined	541	438	137			
Congenital abnormality	9	11	6	ns	ns	0.0535
Spontaneous abortions, sing.	114	109	47	ns	0.0304*	0.0011*
Spontaneous abortions, rec.	35	33	16	ns	ns	0.0389*
Stillbirth, sing.	30	36	17	ns	ns	0.0047**
Stillbirth, rec.	3	6	5	ns	0.0891	0.0027**

B. Age group 20-30	I ^a	II ^b	III ^c	p ^{ab}	p ^{bc}	p ^{ac}
Number of families examined	176	153	15			
Congenital abnormality	1	0	0	ns	nd	ns
Spontaneous abortions, sing.	20	25	4	ns	ns	0.0861
Spontaneous abortions, rec.	0	6	1	0.008**	ns	0.0006**
Stillbirth, sing.	1	6	0	0.0355*	ns	ns
Stillbirth, rec.	0	1	0	ns	ns	nd

C. Age group 31-50	I ^a	II ^b	III ^c	p ^{ab}	p ^{bc}	p ^{ac}
Number of families examined	247	248	74			
Congenital abnormality	5	10	3	ns	ns	ns
Spontaneous abortions, sing.	59	73	24	ns	ns	ns
Spontaneous abortions, rec.	16	23	7	ns	ns	ns
Stillbirth, sing.	15	22	6	ns	ns	ns
Stillbirth, rec.	1	5	1	ns	ns	ns

D. Age group 51-60	I ^a	II ^b	III ^c	p ^{ab}	p ^{bc}	p ^{ac}
Number of families examined	118	37	48			
Congenital abnormality	3	1	3	ns	ns	ns
Spontaneous abortions, sing.	35	11	19	ns	ns	ns
Spontaneous abortions, rec.	19	4	8	ns	ns	ns
Stillbirth, sing.	14	8	11	ns	ns	0.0711
Stillbirth, rec.	2	0	4	ns	0.0721	0.0378*

Table 2. Relative frequencies of reproduction function pathological outcomes in families settled on the sprayed by Agent Orange territory

Pathology	Controls N=251	Binh My village, N=260	
		Total	Born in 1961-1970
Spontaneous abortions /1000 pregnancies	30-40	38	84
Stillbirths /1000 deliveries	5-7	9-10	20
Congenital abnormalities /1000 deliveries	1-2	8	14

The majority of persons from 20-30 age group was born after AO spraying. It appeared possible to find those who suffered direct contacts with war chemicals and could remember this fact but there were only 15 persons of this age in ERG III. It is very difficult to regard

RISK (po)

the single case of recurrent spontaneous abortion in this group as the sign of pathology increase, but the tendency of abortions' frequency enhancement should be taken into consideration. The significance of this fact is increased by the data observed in the total ERG III contingent (table 1, A). The individuals from ERG II (20-30) grew on the contaminated territory and were exposed to DEF from their childhood. The significant increase in reproductive pathology was observed in this group, particularly the frequencies of stillbirths and recurrent abortions ($p < 0.05$).

There were no significant alterations in reproductive function failures among females aged 31-50 according to the exposure. However, this might be the result of the underestimation, as information was collected only by the standard age groups, and the regression analysis was impossible. The figures obtained for the total ERGs prove this fact (table 1, A).

Nevertheless, the differentiation of population according to ERG ⁵⁾ permitted to reveal the higher values of pathologic outcomes' frequencies in ERG III, that is among those with the direct AO exposure. This information required the detalization and testing, so the specialized study was designed aimed on the medical genetical characteristics of population under study.

The questionnaires were collected in Binh My village and in several control villages to obtain the "normal" characteristics of pathological outcomes. Along with the routine questions on miscarriages, stillbirths, molar pregnancies and congenital abnormalities the questionnaires were supplied with those on obstetrics, gynecology and genetics. The questionnaires were filled by the especially trained medical team of the MCH Family Planning Center. Besides, the genealogical data were collected for 180 families (with $\approx 4,000$ members) to reveal the cases of inherited abnormality. The examination of generations available for the study permitted to exclude the inheritable component in the congenital pathology. There was only one case - a family with dominant segregation of 6-fingers.

Results of medical genetical analysis ¹⁾ supported the associative correlation of reproduction function pathology with the direct AO exposure. The decreases in physical maturation rates were found on the sprayed territory as well as frequent irregularity of menses and the general weakness in women's health ^{1,5)}. For example, the highest frequencies of irregular menses have been observed in women born after 1960 in Binh My, and only 10.5% of young women in the same group had an early (before 16) menophania (37% in controls) ¹⁾. In average 30% of women in the sprayed region had problems in child bearing. That were threatened abortions, hypoxia, hypotrophism, etc. The premature births and neonatal diseases may be provoked by the same causes.

The significant positive association was found for the frequency of miscarriages and the IGHS in the ERG III women aged 20-30 ($p = 0.002$). In the control region such association could be seen only in the elder group (31-50, $p = 0.02$). The associations were observed in factor analysis, when the main components of the exposure and effects were analyzed. There were less than 0.7% of women exposed to pesticides in ERG I and ERG III. Those from ERG II ($\approx 5\%$) had the worse levels of IGHS, thus they had stronger correlations of pathologic events with poor health.

These facts coincided with those on the loss of several "years of well-being life" for the whole period of living on the sprayed territory ^{2,6)}. The same might be proved by the frequent prevalence of the cells with nucleus' defects (cells in early apoptosis included) shifted to the younger women's' group ⁷⁾.

An interesting observation on the sprayed territory should be mentioned. The highest frequency (3.5%) of early postnatal deaths' was registered in the ERG II young families

without obvious reproductive failures. At the same time, this value was the lowest - 0.55%, in ERG II females with reproductive abnormalities¹⁾. The fragility of reproduction system and function in most cases results in early fetal death or stillbirth. It might have resulted in early child death in younger women strong enough to bear the fetus.

On the base of obstetrical data the probable frequencies of pathological events were estimated for the group of females born during the 60th - during the war-time and close afterwards. These data are demonstrated in table 2, and they indicate the possible enhancement in abnormal reproductive events among persons exposed to AO during childhood or while embryonic development and to DEF afterwards.

3. Conclusions

The late physical maturation, irregular menstrual cycles (found in 40% of females), chronicle inflammations of the genital tract - all these are the manifestations of the general health weakness in persons exposed to dioxin and/or to DEF. The deteriorated health status may lead to the frequent pathologic events in pregnancies.

The possibility of abnormal pregnancies in persons exposed to DEF should be stressed. This means that population on the sprayed territory is currently at risk of being affected by the environmental ecotoxicological factors. So, the fetus may suffer not only of the dioxin itself, but from the consequences caused by mother's organism fragility.

The data on the levels and profiles of dioxins in human milk on the investigated territory⁸⁾, the results of medical genetical and cytogenetical studies^{1,9)} suggest that the revealed pathologic events in reproduction are associated with the environmental factors' effects. The lack of such abnormalities in upper generations permitted to reject the inherited pathology. Nevertheless, we consider it important to continue the survey to make a perfect conclusion on the realization of the exposure effects.

4. References

1. Huynh T. Kim Chi, Oumnova N., N.Q. An, Roumak V. Genetico-Toxicological Studies in the South Vietnam. 3. Reproduction Function Disturbances in the South Vietnamese Rural Inhabitants. In: The 2nd Int. Symp. "Herbicides in War". Abstr. b. //Hanoi. - 1993. - PP. 215-218.
2. Roumak V., Poznyakov S., Antonyuk V., N.Q. An, Sofronov G. Consistent deterioration of general health status in South and North Vietnamese exposed to Agent Orange //Organohalogen Compounds. - 1995. - 25. - PP. 161-166.
3. Poznyakov S., Roumak V., Oumnova N., N.Q. An, T.X. Thu, Sofronov G., Kountzevitch A. "Dioxin" - hormone-like disadaptogenic supercotoxicant //J. Ecol. Chem. (Publ. Alga-Fund, St. Petersburg). - 1993. - N 2-3. - PP. 179-199.
4. Roumak V., Poznyakov S., Oumnova N., Sofronov G. The experience of the investigations of the ecotoxicological pressure on the rural population of the South Vietnam in the region sprayed by Agent Orange //Organohalogen Compounds. - 1996, this issue.
5. Poznyakov S., Antonyuk V., N.Q. An, T.X. Thu, Kountzevitch A., Sofronov G., Roumak V. The long-term health consequences of Agent Orange in Vietnam: evidences of the reality and medical significance //Organohalogen compounds. - 1994. - v. 21. - PP. - 175-179.
6. Antonyuk V.V. Development of algorithm on medical statistical support for the complex investigations of the Long-Term Medical Consequences of the exposure to dioxin-containing herbicides. Ph. Dr. Thesis //Moscow. - 1995. - 24 PP. (in Russ.).
7. Oumnova N., Zhuleova L., Huynh T. Kim Chi, Roumak V. Application of Micronucleus Test for Indication of the Environmental Factors Clastogenic Activity on the Territory of Song Be Province (South Vietnam) //Organohalogen Compounds. - 1995. - v. 25. - PP. 131-136.
8. Kluyev N.A. (personal communication).
9. Oumnova N., Roumak V., N. Q. An, Sofronov G. Development of Ecogenetic Aspects for the Assay of Long-Term Medico-Biological Consequences of the Agent Orange Exposure //Organohalogen Compounds. - 1995. - 25. - PP. 155-159.