

**122**

БАЛКАНСКИ МЕДИЦИНСКИ СЪЮЗ

НАЦИОНАЛНА СЕКЦИЯ НА БЪЛГАРИЯ

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У Д О С Т О В Е Р Е Н И Е

Ръководството на Националната секция на Балканския медицински съюз удостоверява, че доклад на тема: *L'evaluation electrophysiologique du risque toxicologique chez les tractoristes travaillant avec des pesticides*

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е приет за участие в XXI<sup>ва</sup> Балканска медицинска седмица, която ще бъде проведена от 02 до 05 Септември 1990 г.

Секретар на Националната секция на БМС:

/проф.Ст.Баев/

**L'EVALUATION ELECTROPHYSIOLOGIQUE DU RISQUE TOXICOLOGIQUE  
CHEZ LES TRACTORISTES TRAVAILLANT AVEC DES PESTICIDES**

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Sofia, Bulgarie**

A l'aide de l'analyse mathématique du rythme cardiaque et de la méthode électroneurologique ont été examinés 77 tractoristes dans quelques stations de machines agricoles et de tracteurs, travaillant avec des pesticides. L'examen a été fait doublement - avant et après la saison de pulvérisation. Les résultats obtenus ont été comparés avec ceux des tractoristes d'un groupe de contrôle qui n'ont pas participé à la pulvérisation. On a établi qu'il y a quelques différences importantes entre les deux groupes seulement quant à l'examen fait à la fin de la saison de pulvérisation.

Ces résultats confirment l'hypothèse de la présence d'un certain risque de santé, lié avec ce genre de travail.

**UNION MEDICALE BALKANIQUE  
SECTION BULGARE DE L'U.M.B.  
MINISTERE DE LA SANTE PUBLIQUE ET DE L'ASSISTANCE  
SOCIALE DE LA R.P. DE BULGARIE**



**INVITATION  
XXI SEMAINE MEDICALE BALKANIQUE**

2-5 Septembre 1990

ASSESSMENT OF TOXICOLOGICAL HAZARD BY MEANS OF ANALYSIS  
OF HEART RATE VARIABILITY AND ELECTRONEUROGRAPHY

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INTRODUCTION

Monitoring and control of human exposure to pesticides is Objective 7 of the UNDP-supported project "European cooperation on environmental health of the control of chemicals". The Institute of Hygiene and Occupational Health, Sofia, has been accepted as the lead institution for this Objective within the framework of which an epidemiological study on the health effects of organophosphorous pesticides was planned (Kaloyanova F., 1985).

The neurotoxic effects of organophosphorous pesticides exposure are directly related both to cholinesterase inhibition classified as muscarinic, nicotinic and CNS effects and delayed effects involving pathological conditions on which precise knowledge is still not available. If the primary effects appear after an acute or subacute episode, usually high level exposure, the delayed type may be a consequence of repeated low level exposure.

Neuropathy seems to develop only after massive exposure to organophosphorous compounds (Sapalainen (1988)). Only Roberts (1976) has reported on slower MCVs of the ulnar nerve among eight workers engaged in the development, manufacture, and formulation of an organophosphorous pesticide in comparison to eight nonpesticide factory workers.

In a series of studies, Roberts and et al. (1970, 1972, 1977) has described electrophysiological changes in the absence of detectable blood cholinesterase inhibition among pesticide workers exposed to organophosphorous compounds. The main change they have reported was reduction of the amplitude of the muscle action potential to nerve stimulation, and this was suggested to be a sign of early toxicity suitable for screening of exposed workers. Longitudinal follow-up of exposed workers showed exposure-related fluctuations in the amplitude of the motor response (Roberts 1977). The autor suggested a diphasic effect on EMG amplitude: initially an increase in voltage, and later, when exposure continued, a decrease. On the other hand Kimura (1974) and Stalberg et al. (1978) have not found any effects on the amplitude of the evoked EMG activity.

In recent years the examination of the peripheral autonomic nervous system (ANS) has become an well established part of the hazard-related health screening activity. Autonomic neuropathy has been demonstrated in diabetes and in uremia, but it has been described also in some of diseases affecting peripheral nervous system (PNS).

The aim of this study is to investigate the dysfunction

of ANS and PNS in workers with long - standing exposure to organophosphorous pesticides (OPP).

#### MATERIAL AND METHODS

The chronic toxicity of the OPP was investigated by means of computer analysis of heart rate variability study and electroneurography. The main use of pesticides in Bulgaria is in agricultural enterprises in order to combat with various of them. It is well known that OPP belong to a category which is one of the mostly hazard.

The possibility of damaging the ANS because of occupational exposure to OPP makes it necessary to include in the screening procedure some more reliable tests. Analysis of heart rate variability (HRV) seems to be a convenient method for assessment of the pesticides - related changes in the ANS.

The experiment including HRV analysis was carried out in two stages:

-In the first stage-41 workers engaged in OPP spraying were investigated before spray season and the results obtained were compared with 14 controls;

-In the second stage-36 workers engaged in OPP spraying were investigated at the end of the spray season and the results obtained were compared with 19 controls.

All of the control subjects were tractor drivers and mechanical service workers having no contact with OPP.

Electroneurographic (ENG) investigation has been carried out on three groups of agricultural workers:

-1st. group-24 workers engaged in OPP spraying investigated before spray season;

-2nd. group-24 workers engaged in OPP spraying investigated at the end of the spray season.

-Control group-24 tractor drivers and mechanical service workers.

#### PROCEEDURE

According to the Protocol (adopted on the Consultation on Neurobehavioural Tests, Sofia, 1984) the ENG investigation included the following nerve conduction studies:

-Motor conduction velocity of the median nerve.

-Motor conduction velocity of the peroneal nerve.

-Sensory conduction velocity of the median nerve.

ENG was amplified by means of a portable electromyograph Medicor-Type KTD-3. All subjects were investigated in a room of the medical office.

The parameters of HRV were obtained by ECG signal converted to R - R intervals. Computer facilities were used for calculation of the following parameters: X, SD, S (mean successive positive differences between R-R intervals), N (number of waves in cardiogram), S/N, S.N, Mo, AMo (%), R (the differences between R-R the largest and the smallest R-R interval), indices of tension (T), vegetative ballance (VB), homeostasis (H).

All measurements were made at rest, for a period of 10 minutes.

## RESULTS

Table 1 presents the data obtained in the first and in the second stages of the experiment. As it can be seen the exposure to OPP during the spray season results in an increased tension of the cardiovascular mechanisms taking part in the process of adaptation. From 12 parameters of heart rate variability, four proved to be a sensible instrument for assessment of the toxicological hazard.

The results of the ENG investigations (mean values and standard deviation) are shown in Table 2. As can be seen the conduction velocity of the median nerve (motor and sensory parts) as well as peroneal nerve is significantly lower in the 2nd group of sprayers, when compared with the control group ( $p = 0.001$ ). The conduction velocity of median nerve - motor part, in first group is also lower, when compared with control group ( $p = 0.05$ ).

## CONCLUSIONS

As a result of this study it is difficult to state ultimately that the methods we have used are the best discriminators of OPP health hazard. Nevertheless, some conclusions, concerning before all the methodological aspect of the problem can be made:

1. The use of the parameters of HRV for the purposes of toxicological investigations including OPP exposure seems to be justified. These parameters proved to be a reliable discriminator of the hazard-related ANS disbalance.
2. At the end of the spray season the conduction velocity of the median and peroneal nerves decreased significantly (in comparison with the control group). That means - the ECG following-up have to be a obligatory part of the tests battery, employed when toxicological exposure to pesticides have to be reliable assessed.

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TABLE 1.

HEART RATE VARIABILITY PARAMETERS BEFORE (1) AND AFTER (2)  
SPRAY SEASON

PARAMETER		1		2	
		SPRAYERS	CONTROLS	SPRAYERS	CONTROLS
$\bar{X}$	s	0.90+0.12	0.85+0.08	0.71+0.11*	0.92+0.11
SD	s	0.58+0.30	0.54+0.25	0.32+0.08*	0.59+0.20
S	s	11.0+6.4	11.0+5.8	9.6+5.8	11.0+5.0
N numb.		333+95	339+53	461+106*	363+85
Mo	s	0.94+0.14	0.84+0.09	0.77+0.12*	0.89+0.12
AMo	%	19.4+8.2	20.6+8.0	16.2+5.3**	23.7+7.0
	s	0.22+0.11	0.23+0.09	0.16+0.01*	0.14+0.09
AMo T(-----) 2Mo. R		46.9+41.7	53.3+47.7	65.7+42.4*	55.5+48.4
AMo VB(-----) X. F		98.0+72.3	105.4+88.4	142.4+89.5*	107.3+100.0
AMo H(-----) Mo. SD		35.6+30.4	45.4+33.1	65.7+51.3*	45.1+25.1

St. sign.

\* p < 0.05

\*\* p < 0.01

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N numb.	333+95	339+53	461+106*	363+85
Mo s	0.94+0.14	0.84+0.09	0.77+0.12*	0.89+0.12
AMo %	19.4+8.2	20.6+8.0	16.2+5.3**	23.7+7.0
R s	0.22+0.11	0.20+0.07	0.16+0.01*	0.24+0.09
T (-----) AMo 2Mo. R	46.9+41.7	53.3+47.7	65.7+42.4*	55.5+48.4
VB (-----) AMo X. R	98.0+72.3	105.4+88.4	142.4+89.5*	107.3+100.0
H (-----) AMo Mo. SD	35.6+30.4	45.4+33.1	65.7+51.3*	45.1+25.1

St. sign.

\* p < 0.05

\*\* p < 0.01

TABLE 2.

MEAN VALUES (X, SD) AND STATISTICAL ANALYSIS (STUDENT'S t-TEST) OF E N G DATA.

GRD UP	MEDIAN NERVE (MOTOR)			MEDIAN NERVE (SENSORY)			PERONEAL NERVE		
	AMPL. (mv)	DIST. LAT. (ms)	COND. VEL. (m/s)	AMPL. (v)	DIST. LAT. (ms)	COND. VEL. (m/s)	AMPL. (mv)	DIST. LAT. (ms)	COND. VEL. (m/s)
CONTRD (C)	14.5 0.8	2.1 0.1	63.2 1.1	16.3 1.0	2.5 0.1	61.5 1.9	7.6 0.6	3.3 0.2	50.9 0.7
1st	13.0 0.7	2.2 0.1	61.4* 0.8	17.0 0.6	2.4 0.3	60.5 0.8	8.6 0.6	3.2 0.1	51.1 0.9
2nd	13.1 0.6	2.5 0.2	60.2** 0.7	16.5 0.9	2.8 0.4	58.8** 0.7	7.8 0.5	3.8 0.3	48.2** 0.7

\* p = 0.05 (C/1st)

\*\* p = 0.001 (C/2nd)