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MUT/05/9

**COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD
CONSUMRE PRODUCTS AND THE ENVIRONMENT**

REVIEW OF GENOTOXICITY IN PESTICIDE APPLICATORS

Cytogenetic changes in workers following cumulative exposure to pesticides

Selected studies from EU and world

1. In most biomonitoring studies in which cytogenetic changes following pesticide exposure was studied, quantitative evaluation of exposure is sometimes difficult, hence duration of exposure is often used as a surrogate measure of exposure. In a review of genotoxicity of pesticides, Bolognesi (Bolognesi, 2003) concluded that chronic exposure to low doses of complex mixtures of pesticides induced cumulative cytogenetic effects, as the incidence of chromosome aberrations (CA), micronuclei (MN) and sister chromatid exchanges (SCE) was positively correlated with duration of exposure in a number of studies of farmers and floriculturists that were continuously exposed to pesticides (Bolognesi, 2003, Bolognesi, *et al.*, 1993a, Bolognesi, *et al.*, 1993b, Bolognesi, *et al.*, 2002, Gomez-Arroyo, *et al.*, 1992, Hoyos, *et al.*, 1996, Jablonicka, *et al.*, 1989, Paldy, *et al.*, 1987, Rupa, *et al.*, 1989b, Scarpato, *et al.*, 1996, Shaham, *et al.*, 2001). In contrast, other studies described an increase in cytogenetic damage irrespective of duration of exposure (Kourakis, *et al.*, 1992, Rupa, *et al.*, 1989a, Rupa, *et al.*, 1991). However, as several other studies also stated the lack of correlation between genotoxicity and duration of exposure (Antonucci and de Syllos Colus, 2000, Bolognesi, *et al.*, 2004, Carbonell, *et al.*, 1993, Dulout, *et al.*, 1985, Lebailly, *et al.*, 2003, Lucero, *et al.*, 2000, Nehez, *et al.*, 1988).

2. Previous reports (MUT/05/1) described criteria that were used to select studies that could be used for further evaluation. From the 25 selected studies, five reported a positive correlation between duration of exposure and cytogenetic damage, whereas four studies failed to show such a relationship. The remaining 14 studies did not report appropriate data.

3. The relationship between duration of exposure and cytogenetic damage for the selected studies are presented in table 1.

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Floriculturists

4. Bolognesi and colleagues reported a dose-response relationship between duration of exposure and MN frequency in floriculturists employed for 19-30 and > 30 years (Bolognesi, *et al.*, 1993b). In contrast, in a more recent study of floriculturists, MN frequency was not significantly increased with duration of exposure (Bolognesi, *et al.*, 20049). Similarly, CA were not significantly different in floriculturists undergoing acute or chronic exposure (Dulout, *et al.*, 1985).

Agricultural workers and farmers

5. Agricultural workers occupationally exposed for > 10 years to pesticides had a significantly higher frequency of CA than controls or those exposed for shorter periods (Carbonell, *et al.*, 1993). Moreover, a linear increase in MN frequency with years of exposure was reported for farmers being exposed for <19 or > 19 years (Pasquini, *et al.*, 1996).

Production workers

6. A small but significant increase in comet tail length was seen in production workers occupationally exposed to pesticides > 10 years compared to those with shorter lengths of exposure (< 10 years) (Grover, *et al.*, 2003). In contrast, following their study in production workers exposed to pesticides for 0-10 or 10-20 years, Antonucci and colleagues concluded that the frequency of CA was not correlated with exposure time to pesticides (Antonucci and de Syllos Colus, 2000).

Pesticide sprayers

7. In Hungarian mixers and sprayers, there was a trend for CA to increase with duration of exposure, the frequency of CA being higher than controls after 0-5 years of exposure and longer (Paldy, *et al.*, 1987). In contrast, there was no correlation between the frequency of CA and the duration of exposure in pesticide sprayers working in greenhouses (Kourakis, *et al.*, 1992). Moreover, the CAs observed in workers spraying cotton-fields was increased following pesticide exposure, irrespective of duration of exposure (Rupa, *et al.*, 1991).

Conclusion

8. Five studies report a correlation between duration of exposure and cytogenetic damage. However, from the available data, there is only evidence of a marginal time response relationship.

9. To conclude, from the 25 selected studies, there is no convincing evidence to suggest that cumulative exposure to pesticides increases cytogenetic damage.

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Table 1: Evidence of cumulative exposure in the selected studies.

Subjects (exposed/controls)	End-point	Cytogenetic damage following cumulative exposure	Magnitude of response – fold increase	Author
Production workers (23/23)	CA	Negative CA was not correlated with duration of exposure, in two exposure groups studied (0-10 and 10-20 years)	0-10 years = 0.9 10-2 years = 1.1	Antonucci and de Syllos Colus, 2000
Agricultural worker (20/20)	CA Tandem probe FISH assay	Not studied		Au, <i>et al.</i> , 1999
Italian floriculturist (71/75)	MN	Positive. MN frequency increased with duration of employment. Three groups studied: 1-18, 19-30 and > 30 years.	1-18 years = 0.8 19-30 years = 1.3 > 30 years = 1.7	Bolognesi, <i>et al.</i> , 1993b
Italian floriculturist (51/24)	MN	Negative No significant correlation was seen between MN and duration of exposure. Two groups studies: < 20 and > 20 years.	< 20 years = 1.2 > 20 years = 1.3	Bolognesi, <i>et al.</i> , 2004
Spanish agricultural worker (70/69)	CA and SCE	Positive Workers exposed for > 10 years had a significantly higher frequency of CA. Five groups studied: <5, 5-9, 10-19, 20-29 and >29.	<5 years = 1.1 5-9 years = 1.2 10-19 years = 1.5 20-29 years = 1.5 >29 years = 1.6	Carbonell, <i>et al.</i> , 1993

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Spanish agricultural worker (29/53)	CA	Not studied		Carbonell, <i>et al.</i> , 1995
Italian floriculturist (32/32)	CA and SCE	Not studied		De Ferrari, <i>et al.</i> , 1991
Floriculturist (36/15)	CA	Not studied		Dulout, <i>et al.</i> , 1985
Pesticide sprayers (23/18/20/33)	Not stated	Not studied		Garry, <i>et al.</i> , 1996
Forester (25/15)	CA	Not studied		Garry, <i>et al.</i> , 2001
Production workers (54/54)	Comet assay	Positive A small but significant increase in comet tail length was seen between workers with < 10 years exposure and those with > 10years exposure.	<10 years = 2.2 >10 years = 2.3	Grover, <i>et al.</i> , 2003
Agricultural worker (30/30)	CA	Not studied		Hoyos, <i>et al.</i> , 1996
Czech production workers (44/30)	CA and SCE	Not studied		Jablonicka, <i>et al.</i> , 1989
Yugoslavian pesticide sprayer (27/15/20)	CA, SCE and MN	Not studied		Joksic, <i>et al.</i> , 1997
Greek pesticide sprayer (29/14)	CA	Negative No significant correlation between duration of exposure and CA. Three groups studied: 4-10, 11-17 and 18-30 years.	4-10 years = 5.6 11-17 years = 4.8 18-30 years = 3.3	Kourakis, <i>et al.</i> , 1992
Finnish greenhouse worker (116/29)	CA	Not studied		Lander, <i>et al.</i> , 2000

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French fruit farmer (19)	Comet assay	Not studied		Lebailly, <i>et al.</i> , 2003
Pesticide sprayers (9/7/6)	CA	Not studied		Mohammad, <i>et al.</i> , 1995
Italian greenhouse workers (57/33)	³² P DNA post-labelling	Not studied		Munna, <i>et al.</i> , 1999
Finnish forestry workers (19/15)	CA	Not studied		Mustonen, <i>et al.</i> , 1986
Hungarian pesticide sprayer (80/24)	CA	Positive Frequency of CA was significantly correlated with duration of exposure. Four groups studied: 0-5, 6-10, 11-15 and >15 years.	0-5 years = 2.7 6-10 years = 3.2 11-15 years = 3.9 >15 years = 2.7	Paldy, <i>et al.</i> , 1987
Italian farmer (48/50)	SCE and MN	Positive There was a linear increase in MN frequency according to years of exposure. Two groups studied: < 19 and > 19 years.	<19 years = 1.1 >19 years = 1.4	Pasquini, <i>et al.</i> , 1996
Floriculturist (41/41)	CA	Not studied		Paz-y-Mino, <i>et al.</i> , 2002
Italian greenhouse floriculturist (26/22)	³² P DNA post-labelling	Not studied		Peluso, <i>et al.</i> , 1996
Pesticide applicators (26/26)	Not stated	Negative No significant correlation between CA and duration of exposure. Four groups studied: 2-5, 6-10, 11-15 and 16-18 years.	0-5 years = 3.4 6-10 years = 3.7 11-15 years = 3.7 16-18 years = 3.4	Rupa, <i>et al.</i> , 1991

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