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ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE LISBOA

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CENTRO DE INVESTIGAÇÃO E ESTUDOS EM SAÚDE PÚBLICA

OCCUPATIONAL EXPOSURE TO FORMALDEHYDE: EFFECTS OF YEARS OF EXPOSURE IN THE FREQUENCY OF MICRONUCLEUS

Carina Ladeira, Susana Viegas, Carla Nunes, Joana Malta-Vacas, Mário Gomes, Paula Mendonça, João Prista, Manuel Gomes, Miguel Brito

Finland, 6 September 2010

FORMALDEHYDE

- *Formaldehyde: an important industrial compound used in the manufacture of synthetic resins and chemical compounds such as lubricants and adhesives*

- *Also applied as a disinfectant, preservative and in cosmetics productions*

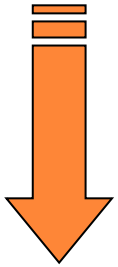
- *Relevant workplace exposure to FA also occurs in anatomy, pathology and in mortuaries*

(WHO, 1989; IARC, 2006; NICNAS, 2006)

FORMALDEHYDE

- *Classified by IARC as carcinogenic to humans (Group 1), based on sufficient evidence in humans and experimental animals*

- *Manifold in vitro studies indicated that FA can induce genotoxic effects in proliferating cultured mammalian cells*



Micronucleus Test

MICRONUCLEUS

- *Represent true mutagenic events*
- *Increase use in biomonitoring studies*
- *Originate from chromosome fragments or lagging whole cromossomes*
- *Are a sensitive indicator of damage to chromosomes or the mitotic spindle*
- *MN belong to the most sensitive genetic endpoints for the detection of FA induced genotoxicity*
  (Merk e Speit, 1998)

MICRONUCLEUS

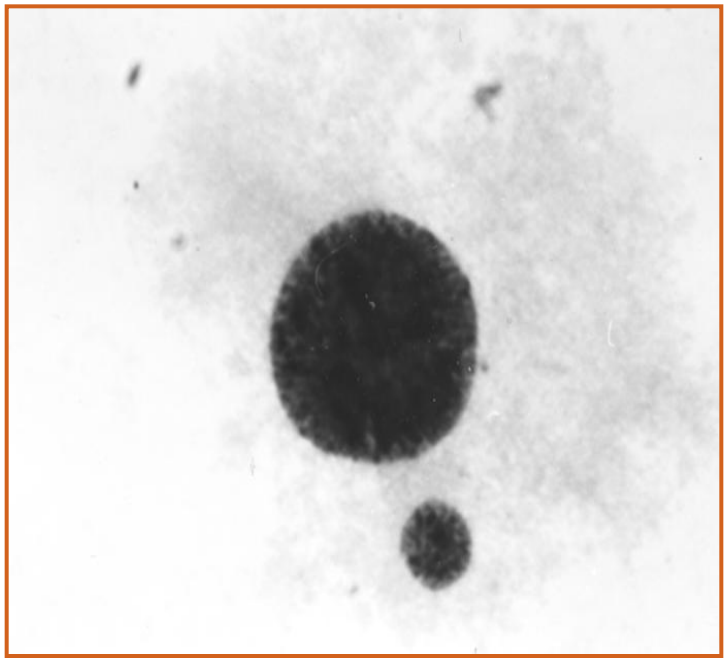


Figure 1 - MN in exfoliated cell

Source: Fenech et al., 2003

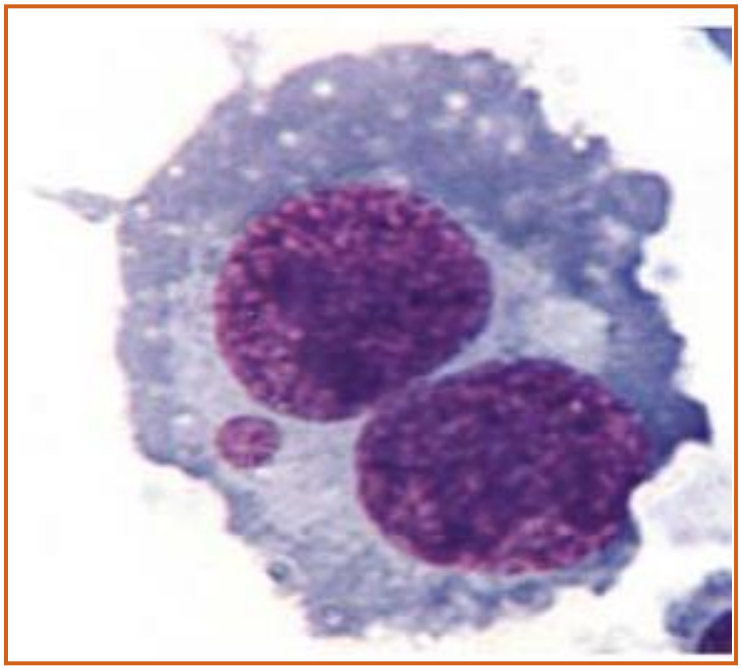


Figure 2 - MN in peripherial blood lymphocyte

Source: Fenech et al., 2003

STUDY DEVELOPED

Aim of the study:
to evaluate if years of exposure induced a genotoxic biomarkers increase, namely MN in lymphocytes and buccal cells, in workers occupationally exposed to FA (factory and pathology anatomy laboratory)

The following actions were developed:

- *Formaldehyde environmental monitoring*
- *Genotoxic effects evaluation by application of:*
  - *MNT in the epithelial cells from buccal mucosa*
  - *MNT in peripherial blood lymphocytes*

Photo Ionisation Detector

Source: Ion Science

STUDY DEVELOPED

- *A study was carried out in Portugal in 80 workers: 30 workers in a FA production factory and 50 in ten pathology and anatomy laboratories*
- *A control group of 85 non-exposed subjects*
- *The subjects read and signed an informed consent form*
- *Subjects with a recent medicine history were excluded from the study*

MATERIALS AND METHODS
Environmental Monitoring of FA exposure

- *The values of FA in the ceiling were obtained from instantaneous measurements. This monitoring was performed using Photo Ionisation Detection equipment with simultaneous video recording*

- *This method:*

- *Allows direct association between worker activities and ceiling values.*
- *Provides hints on the main exposure sources*

(McGlothin, et al., 2005)

MATERIALS AND METHODS
Micronucleus Assay

Peripheral Blood Lymphocytes

- *Culture of lymphocytes and Cytokinesis-Block Micronucleus Assay*
- *May-Grünwald Giemsa technique*
- *Observed 1000 lymphocytes from peripheral blood per individual*

Buccal mucosa

- *Cells from the buccal mucosa were sampled by endobrush*
- *Exfoliated cells were smeared onto slides and used Feulgen technique*
- *Observation of 2000 cells per individual from buccal mucosa*

RESULTS

Table 1 - Characterization of the studied population

	Control Group	Exposed Group	*P* value
Number of subjects	85	80	
Gender Male Female	31 (36.6%) 54 (63.5%)	48 (60.0%) 32 (40.0%)	0.002
Age (years) Range Mean St. Deviation	20-55 33.87 8.262	19-56 35.74 9.470	0.180 0.024
Smoking status Non-smokers Smokers	59 (69.4%) 26 (30.6%)	55 (68.8%) 25 (31.3%)	0.927
Years of exposure Range	------	1 – 35	

RESULTS

Table 2 - FA exposure in the two occupational settings

	Factory	Laboratories
Exposure duration (Years) **Range** **Mean** **St. Deviation**	 1 - 27 6.2 6.74	 1 – 33 14.5 9.12
Working hours/day (h)	7	7
FA ceiling concentration (ppm) **Range** **Mean**	 0.003 – 1.04 0.52	 0.02 – 5.02 2.52

RESULTS

Table 3 - Frequency of MN in the studied population

	Controls	Exposed		
		Factory	Pathology and anatomy laboratories	Total
MN PBL Mean Std. Dev	1.17 1.95	1.76 2.07	3.70 3.86	2.97 3.42
MN EBC Mean Std. Dev	0.13 0.48	1.27 1.55	0.64 1.74	0.88 1.69

p<0.001

RESULTS

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***p*=0.16**

***p* < 0.001**

RESULTS

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p<0.001

***p* < 0.005**

RESULTS

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p<0.005 **p=0.108**

RESULTS

Table 4 - Correlation analysis between genotoxic endpoints and years of exposure (Spearman's test)

Genotoxic endpoints	Years of Exposure
MN PBL	r = 0.401 $p < 0.001$
MN EBC	r = 0.209 $p = 0.008$

CONCLUSIONS

- *Both groups of workers (factory and laboratory) were exposed to high peak concentrations. This is important because…*
- *… health effects resulting from FA exposure relate more to peaks of high concentrations than to long time exposure at low levels (IARC, 2006; Pyatt et al., 2008)*
- *MN in lymphocytes showed a potential genotoxic damage in subjects with long-exposure to FA* (Ye et al., 2005)
- *MN in buccal cells showed local genotoxic effects from the first contact of FA (Burgaz et al., 2002 & Speit, 2006)*

CONCLUSIONS

- *There is a moderate positive correlation between MN frequency (both in peripheral blood lymphocytes and in epithelial buccal cells) and the duration of FA exposure (years of employment)*
- *Years of exposure are also influent upon the development of health effects*
- *There was a long-term exposure to high levels of FA especially in pathology and anatomy laboratory workers. This may partially explain the higher frequency of MN in peripheral blood lymphocytes in this group when compared to the factory*

The association of these cytogenetic effects with FA exposure gives important information to risk assessment process and may also be used to assess health risks for exposed groups

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