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Results of Sputum Cytology among Workers Exposed to Vinyl Chloride Monomer and to Poly(vinyl Chloride)

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The results of systematic cytological sputum examinations of 3,380 Italian VC-PVC industry workers and of 2,287 workers in other industries at different potential risk and chosen as control groups are reported.

The results indicate an increase in cellular abnormalities and dysplasias in the epithelium of the respiratory tract among VC-PVC workers. These data are in line with experimental results showing that VC produces lung tumors in mice and with early epidemiological evidence among exposed workers.

Introduction

In 1975, it was decided to include the cytological examination of sputum in the protocol of systematic medical surveillance of the workers in all the Italian plastic factories exposed to vinyl chloride (VC) and poly(vinyl chloride) (PVC).

This program was co-sponsored by the Italian Federation of Unions of Chemical Workers (FULC) and by the Public Health Service of the Italian regions where the factories were located.

The decision to investigate cytologically all Italian VC-PVC industry workers was taken on the basis of the following facts: (1) the observation of a marked increase in the incidence of lung adenomas in mice exposed by inhalatory route, to a spectrum of doses of VC ranging from 10,000 down to 250 ppm (*1-3*); (2) the unusual finding of cellular abnormalities in a high portion of the lung adenomas of exposed mice (*1-3*); (3) the observation of frequent severe abnormalities (squamous dysplasia and atypical adenomatous hyperplasia) in the sputa of a small group of heavily exposed workers (*3*); (4) the report of some increase in lung carcinomas among workers from two VC-PVC factories (*4*); (5) the finding that the majority of lung carcinomas observed among exposed workers were not of a common histotype i.e., giant cell carcinomas (*5*).

Planning and Methods

The investigation was carried out on workers from 13 Italian VC-PVC factories located in the northern, central and southern parts of Italy, namely, in Villadossola (1), Portomarghera (3), Bollate (1), Ferrara (1), Ravenna (1), Rosignano (1), Terni (1), Brindisi (1), Ferrandina (1), Porto Torres (1) and Cagliari (1).

A total of 3380 workers was examined. These workers have been and/or are exposed to the monomer and part of them also to PVC dust. For comparison 2287 workers in other industries at different potential risk were examined: namely, workers manufacturing PVC products, workers in chemical industries not dealing with plastics, metal workers, miners and workers in the chromium industry.

For each sputum examination four cytological slides were prepared. The smears were stained by the Papanicolaou technique.

The slides were screened and evaluated independently by the pathologists of the hospitals in the area where the factories were located, then by a trained cytologist in our institute. All abnormal smears were reviewed by the senior pathologist of

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Table 1. Type, sequence and classification of local changes in the genesis of the various histotypes of pulmonary carcinomas.

Stage					Cytologic classes
		Normal respiratory epithelium			
		Nonciliated cuboid epithelium			
Initial nonspecific stage		Adenomatous hyperplasia	Squamous metaplasia ⇄	Basal cell hyperplasia	II, II-(III) II-III
Intermediate specific state		Atypical adenomatous proliferation	Squamous dysplasia ⇄	Basaloid cell dysplasia	(II)-III, III, III-IV
Tumor stage	Preclinical tumor	*In situ* adenocarcinoma	*In situ* squamous carcinoma	*In situ* anaplastic carcinoma	IV and V
		Invasive adenocarcinoma →	Invasive squamous carcinoma →	Invasive anaplastic carcinoma	
	Clinical tumor	→	→	→	

Table 2. Classification, characterization, distribution by classes and code of sputum cytology findings.

Class	Cell character: Type[a]	Degree	Quantity	Code
Not performed				99
I	Normal epithelium (LRE, URE, OCA)		1, 2, 3	01
	Histocytes		1, 2	
I-II	Normal epithelium (LRE, URE, OCA)		1, 2, 3	02
	Histocytes		3	
II	Squamous metaplasia LRE	+/+ +	1, 2, 3	03
	Hypersecretive mucous cells			
II-(III)	Squamous metaplasia LRE	+ + +	1, 2, 3	04
	Adenomatous hyperplasia LRE			
II-III	Mild atypical adenomatous hyperplasia LRE		1	
	Mild squamous dysplasia LRE		1	05
	Mild dysplasia URE, OCA		1	
(II)-III	Mild atypical adenomatous hyperplasia LRE		2, 3	
	Mild squamous dysplasia LRE		2, 3	06
	Mild dysplasia URE, OCA		2, 3	
III	Well defined atypical adenomatous hyperplasia LRE			
	Well defined squamous dysplasia LRE			07
	Well defined dysplasia URE, OCA			
III-IV	Grave atypical adenomatous hyperplasia LRE			
	Grave squamous dysplasia LRE			08
	Grave dysplasia URE, OCA			
IV	Adenocarcinoma			
	Suspected Squamous carcinoma			09
	Undifferentiated carcinoma			
V	Adenocarcinoma			
	Squamous carcinoma			10
	Undifferentiated carcinoma			
Not evaluable				11

[a]LRE = lower respiratory epithelium; URE = upper respiratory epithelium; OCA = oral cavity.

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Table 3. Incidence of various types of cytological changes in sputa: comparison of results among VC-PVC workers and workers of the reference groups.

Group	No. of cases	Non-evaluable cases (insufficient material)	Evaluable cases	Cases without epithelial changes		Cytological changes: Hypersecretive mucous cells and squamous metaplasia LRE +/+ +		Squamous metaplasia LRE + + +		Squamous metaplasia with horn pearls LRE		Adenomatous hyperplasia LRE		Atypical adenomatous hyperplasia LRE		Squamous dysplasia LRE		Dysplasia URE, OCA	
				No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Workers of VC-PVC industry	3380	822	2558	799	31.2	1153	45.1	374	14.6	70	2.7	794	31.0	38	1.5	219	8.6	44	1.7
PVC manufacturers	422	79	343	99	28.9	253	73.8	36	10.5	1	0.3	74	21.6	4	1.2	4	1.2	1	0.3
Workers of various chemical industries[a]	1019	130	889	165	18.6	604	66.9	83	9.3	3	0.3	227	25.5	8	0.9	10	1.1	–	–
Metal workers	264	54	210	73	34.8	109	51.9	30	14.3	1	0.5	5	2.4	–	–	6	2.8	–	–
Miners[b]	402	48	354	47	13.3	254	71.7	41	11.6	1	0.3	59	16.7	5	1.4	4	1.1	1	0.3
Workers of chromium industry	180	28	152	9	5.9	89	58.5	69	45.4	1	0.6	7	4.6	6	3.9	28	18.4	–	–

[a]Other than VC-PVC and chromium industries and not exposed to a known risk.
[b]Not exposed to a known risk.

Table 4. Distribution, by classes of cytological changes in sputa: comparison of results among VC-PVC workers and workers of the reference groups.

Group	No. of cases	Not evaluable cases (insufficient material)	Evaluable cases	Classes: I, I-II		II		II-(III)		II-III		(II)-III		III		III-IV		IV		V	
				No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Workers of VC-PVC industry	3380	822	2558	799	31.2	705	27.5	780	30.4	211	8.6	21	0.8	35	1.3	7	0.2	–	–	–	–
PVC manufacturers	422	79	343	99	28.9	135	39.3	102	29.7	4	1.2	1	0.3	1	0.3	1	0.3	–	–	–	–
Workers of various chemical industries[a]	1019	130	889	165	18.6	399	44.8	313	35.2	6	0.7	6	0.7	–	–	–	–	–	–	–	–
Metal workers	264	54	210	73	34.8	102	48.6	28	13.3	6	2.8	–	–	1	0.5	–	–	–	–	–	–
Miners[b]	402	48	354	47	13.3	220	62.1	82	23.1	2	0.6	1	0.3	1	0.3	1	0.3	–	–	–	–
Workers of chromium industry	180	28	152	9	5.9	63	41.5	51	33.6	18	11.8	2	1.3	5	3.3	4	2.6	–	–	–	–

[a]Other than VC-PVC and chromium industries and not exposed to a known risk.
[b]Not exposed to a known risk.

Table 5. Distribution of classes II-(III) and over among VC-PVC workers and the workers in reference groups.

Groups	Classes II-(III), %	Classes II-III, (II)-III, %	Classes III, III-IV, %
Workers of VC-PVC industry	30.4	9.4	1.5
PVC manufacturers	29.7	1.5	0.6
Workers of various chemical industries	35.2	1.4	–
Metal workers	13.3	2.8	0.5
Miners	23.1	0.9	0.6
Workers in chromium industry	33.6	13.1	5.9

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the same institute. A joint critical reevaluation was carried out for those cases where there was not full agreement.

The same criteria of classification of the lesions and their distribution by classes were adopted by all pathologists.

Such criteria are based on our knowledge of the local cytological changes and of their sequence in the genesis of the various histotypes of pulmonary carcinomas (Table 1).

The list of the most relevant changes correlated with environmental and occupational exposure, their distribution by classes following qualitative and quantitative parameters, and the code, are given in Table 2. This list takes into account not only cells from the pulmonary tree, but also cells from the upper respiratory tract and oral cavity.

Results

The number of valuable cases, the distribution of the cytological changes and the distribution of the results expressed by classes in the group of workers in the VC-PVC industries and in the control groups, are given in Tables 3 and 4. The incidence of dysplastic changes is particularly high in the plastics industry workers when compared to the other control groups, with the exception of chromium workers, which can be considered a positive control. The situation is well illustrated by the distribution of classes II-(III) and above (Table 5).

It may be stated that, in relation to the incidence of respiratory cell abnormalities, the workers in the VC-PVC industries can be placed halfway between chromium workers and other groups.

A finding which deserves attention is the occurrence of atypical cells in the oral cavity and upper respiratory tract in 44 workers (17%) among VC-PVC workers (Table 3).

The results were highly homogeneous in different factories, suggesting that variations in climate, which may affect the incidence of common pneumopathies, is not a determining factor.

The difference in the distribution of the pathological findings was not dependent on tobacco smoking.

Conclusions

The results presented are consistent with experimental data and early epidemiological evidence on the potential oncogenic effects of VC exposure on the lungs.

Furthermore, our data suggest a possible oncogenic risk for the upper respiratory tract which should now be explored by proper epidemiological investigation.

Much remains to be done to clarify the part played by the monomer and by polymer dust in determining the observed cytological changes. Our data are now being re-examined, on the basis of the complete exposure history of single workers, to better establish the role played by PVC particles.

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