IMPERIAL CHEMICAL INDUSTRIES LIMITED
PLASTICS DIVISION

PVC DUST

Paper for APME Meeting in Vienna, 9 June

1 Introduction

Over the past 1/2 years I have from time to time given brief oral reports at CEFIC/APME VCM meetings on the work done by Dr C Wagner of the Pneumoconiosis Research Unit (PRU) of the Medical Research Council (MRC), a UK Government institution. Dr Wagner found that he could generate Kupffer cell sarcomas in rats given intra-pleural injections of emulsion type PVC polymer. On 31 January 1978, the Chemical Industries Association (CIA) had a meeting with various UK Government Departments, the Trades Union Congress (TUC) Medical Adviser and the PRU represented by its new director Dr P Elmes and Dr C Wagner. Partly arising from that 31 January meeting, there was an Ad Hoc Tripartite (ie Government, Union and Industry) Medical Meeting on 5 May at which a serious attempt was made by our Government Employment Medical Advisory Service (EMAS) to persuade industry to accept a change in the status of PVC dust for hygiene purposes. I thought you should know of this since any action by the UK Government in this field could have repercussions elsewhere.

2 Papers on PVC Dust

I attach for your attention a copy of a paper I wrote for 5 May giving a summary of the CIA Meeting of 31 January 1978 (Appendix 1). I also append a copy of a literature summary by Dr M Greenberg of EMAS (Appendix 2). In case you have not seen it, there is also appended (Appendix 3) a copy of a paper by Prof. Arnaud in Thorax (1978 Vol 33 pages 19-25), a journal whose editorial board includes Dr Elmes and Dr Wagner. (Indeed Dr Elmes drew my attention to the paper.) Dr Garlanda has also given me a copy of a summary in English of the Italian trade union epidemiological survey (Appendix 4) and you will note on page 3 reference to 23 pneumoconiosis cases alleged to have been found in men exposed to PVC dust in bagging operations etc.

At the 5 May meeting, Dr D P Duffield gave an oral account of the full chest x-ray studies done by the National Coal Board's radiography unit on 324 ICI workers. He also gave an oral account of recently completed work at an ICI Paints Division plant which compounds and fabricates PVC emulsion polymer. We hope to produce some written reports of this work in the near future despite the fact that we expect our Government to be critical of the work because of inadequate control populations and suggestions that the populations may be of the wrong size and may count as selected populations. Dr D P Duffield and Dr B W Duck referred to work done by European and US companies on chest x-rays - EMAS were not much impressed since no papers have so far been published.

Dr Duffield and Dr Duck criticised the papers listed by Dr Greenberg as being utterly inadequate. Dr Duck told of his frustrations in trying to speak with Prof. Frongia. Both admitted that the Arnoud paper was the first paper we had seen which was well written and merited really close attention. We were also aware that here and there, now and again there

have been isolated single cases of some pulmonary problems which could conceivably be associated with PVC dust. We also know of the University of Louisville's ongoing research into pleural plaque formation in a group of BF Goodrich employees who have been exposed to a number of chemicals including, we believe, VCM but we are uncertain whether they were exposed to PVC dust. We could not believe that 23 pneumoconiosis cases could have occurred in Italy without our Italian friends having told us about them. The TUC Medical Adviser had no information on this point from Italian unions. Moreover we had not had an opportunity so far to inspect or assess Dr Wagner's work on which we have had only interim, oral reports. Furthermore no one knew the significance of intra-pleural injection of any particulate matter as a technique for prediction of ill effects in man and Dr Wagner's latest experiments on PVC dust inhalation must be recognised as difficult work to interpret and monitor both with regard to concentrations of dust and the combination of inhalation plus ingestion which occurs.

EMAS thought there had been sufficient indications over the past 4 years to cast some doubts on PVC dust. In their view there was increasing evidence that the retention of PVC polymer was not a benign process. EMAS moved away from their position of 31 January and suggested to us that the TLV for PVC dust should be reduced from 10 to 5 mg/m^3. We would not accept that there was sufficient medical or biological evidence to warrant such a change. As an alternative EMAS thought that a "best practicable means" approach may be required to improve hygiene. Monitoring of course is a problem here - our measuring methods relate to occasional sampling and we may have to adopt to a sequential monitoring system as for VCM.

There will be further discussions on this matter in June and we can safely predict that our Government and Unions will not be easily satisfied. We are trying to get our work properly written up and presented to EMAS and we will need to improve on measurement procedures. We will discuss yet again with EMAS the need for a morbidity and or mortality study, particularly in the PVC fabrication industry. I am confident that we can take care of these matters in the PVC manufacturing industry if there is an insistence on a best practicable means approach - I am apprehensive about the ability of some parts of the PVC fabrication industry to cope with eg dust monitoring. (In the last day or two I have heard that EMAS have been called in to one of our larger customers and it is alleged a high level of emulsion polymer dust 40 mg/m^3 was found!)

3 Liver Angiosarcoma in the PVC Fabrication Industry

EMAS are investigating an ASL case in a man who was employed for over 30 years in plastics fabrication where, it is alleged he handled polythene, polystyrene and PVC. EMAS were not in a position yet to discuss detail with us but already they were beginning to adopt a stance that there is growing suspicion that low levels of VCM may give risk to ASL. We could not agree that there was "growing suspicion" of this sort. I do not think this ASL case was affecting the EMAS judgement on PVC powders.

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JS/MJE/DSO-107
11 May 1978

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APPENDIX 1

PAPER FOR EMAS MEETING, 5 MAY 1978 AT REGINA HOUSE

PVC DUST

1 Summary Note on Meeting with MRC Pneumoconiosis Research Unit 31 January 1978

Introduction

Under CIA auspices, a meeting was held on 31 January 1978 with HSE, EMAS, DHSS, TUC, BIBRA and CIA representatives present to discuss the MRC work on PVC dust. The following points arose.

(a) Dr Wagner of the MRC in August 1975 gave 48 rats a single intra pleural injection of 20 mgm of PVC emulsion polymer in saline. Between 12 and 18 months, 9 animals died and of these 5 had liver tumours. Pathologists agree 3 tumours were malignant, arising from Kupffer cells. One tumour occurred at the injection site. Nothing further was found until rats 33-45 died and showed liver and spleen fibroses and Kupffer cell damage. 3 animals still survive.

(b) In January 1977, Dr Wagner exposed 48 rats to inhale an atmosphere containing 12 mg/m^3 PVC emulsion polymer dust for 7 hrs day/5 days week for 5 months. In June 1977, 6 exposed rats were sacrificed and evidence found of dust deposition in macrophages in the alveoli, lung tissue, liver and spleen. In January 1976, a further 6 rats were sacrificed and found to have interstitial fibrosis and multiple granulomata in lungs, aggregates of dust around splenic vessels and occasional particles in Kupffer cells in the liver.

(c) In post mortem examinations of human cases in the Llandough Hospital, Dr Wagner found PVC particles in lungs and liver of a man who died from Kupffer cell sarcoma, PVC in the liver of a man who died from a liver tumour, PVC particles in liver and spleen (and interstitial fibrosis) in a man who died from bleeding oesophagal varices and PVC particles in lungs and spleen of a South Wales factory employee who died of bronchitis and emphysema.

(d) Dr Pigott of ICI's CTL described in vitro and in vivo experiments with PVC powders. In vitro, emulsion polymers were cytotoxic when some specific surfactants were left on the particles' surface. Intraperitoneal and intratracheal injection of emulsion polymers into animals showed no response after 6 months. Dr Pigott concluded the PVC powders he had tested in this way were unlikely to produce fibrosis in man.

(e) Dr Elmes and Dr Wagner thought it was too early for Dr Pigott to draw such a conclusion. Moreover there was scattered clinical evidence in the literature to support the possibility that PVC dust may be fibrogenic but Dr Elmes agreed an epidemiological survey would be required to prove this. All agreed that such a survey could not be warranted on the basis of the present evidence.

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(f) Dr Elmes considers that PVC emulsion polymer may contain a diffusible carcinogen and the toxic effects are due to PVC particles and not VCM. The "material" may be a potential cause of lung fibrosis and also liver fibrosis and portal hypertension. Dr Elmes was reminded that the NCB Pneumoconiosis Unit has x-rayed 324 ICI exposed workers and found no cases of dust reticulosis. We also know that Shell and UCC inter alia have x-rayed exposed workers with the same result. Dr Wagner made reference to pleural plaque he had been shown in Goodrich workers - the University of Louisville is examining some 2 dozen cases but their task is difficult since the men seem to have been exposed to chemicals other than VCM and PVC.

(g) MRC would like to do further inhalation work in this area and the CIA promised all possible help. The MRC inhalation facilities are overloaded at the present time and work on another strain of rat would be difficult to accommodate. The CIA would examine what if anything they could arrange in this area. Dr Douglas thought valuable information will probably appear from the existing work in 6 months time.

(h) Dr Wagner would like to have access to other samples of human tissues to check for PVC particles. He also had plans for a series of interlocking experiments to detect synergism with eg barbiturates since many of the South Wales workers who developed liver disease were taking barbiturates or large amounts of alcohol but Dr Fairweather questioned the value of such complex protocols.

(i) The TLV for nuisance dusts in 10 mg/m^3. Mr Henning considered 1 mg/m^3 for the respirable fraction a reasonable target and urged that it would be prudent to improve hygiene here. In fact the respirable fraction in bagging and drying areas averages 1 mgm/m^3. (Dr Wagner's experiments were done at 12 mgm/m^3.) There was no case at present to change the existing "nuisance dust" classification for PVC.

(j) It was agreed that industry would consider the matters brought up at this meeting and at an appropriate stage discuss future action with Dr Douglas and Mr Henning.

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JS/MJE/DSO-107
19 April 1978

PULMONARY DISEASE IN THE VCM/PVC INDUSTRIES

INTRODUCTION

1. Three potential hazard areas can be defined based on the materials to which workers are exposed, namely 1) the polymerization process, 2) the mixing processes, 3) the fabrication processes.

2. In the polymerization processes there is the potential for a worker to be exposed to monomer and/or polymer, depending on the type of process and the stage of the process to which he is exposed. To this may be added exposure to other materials involved in the reaction and to other products of the reaction.

3. A wide range of materials may be met with in the mixing processes where PVC is compounded to produce the material for the particular application that the resin is required for. Among them may be substances that in their own right are known to be associated with respiratory disease.

4. In the fabrication stage, apart from moulding, there may be turning, polishing, welding, bonding, thread-tapping and milling. In these processes a hazard may result if there is thermal degradation or ther is production of fine air-borne particles.

Respiratory morbidity in polymerization workers

5. Miller et al (1975) studied pulmonary function in workers exposed to vinyl chloride and polyvinyl chloride and demonstrated high prevalence of air-flow impairment which increased with age or years of exposure.

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5. continued

They commented on other possible factors and stated that further study would be required to elucidate the effect of general environmental pollution. To date further studies have not been reported by them.

In a further analysis, Miller (1975) separated the effect of occupational exposure and found it to predominate over the effects of smoking.

6. Lilis et al (1976), studying a larger group, observed chest x-ray change and pulmonary function abnormalities that did not always correspond with each other. Respiratory symptoms were also stated to be more common.

7. Wegman (1975) in a conference discussion referred to a small population said to have a pure PVC exposure. Among abnormalities noted three had chest x-rays with fine nodular changes and four had abnormal FEVs and three abnormal FVCs. A scientific publication has not yet been received.

8. Suciu et al (1975) described bronchitic symptoms and emphysema in workers exposed to VCM as well as adverse effects on lung vol.. ventilation and radiographic abnormalities. They concluded that the pulmonary effects were not as intense as other effects and might be caused by other factors such as dust, acids or bases.

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9. Gamble J et al (1976) studied vinyl chloride polymerizers and rubber workers but were unable to repeat the observation of Miller et al. They raised the points of the possible differential migration of susceptible workers from their populations and the shortcomings of the internal comparisons they had made between various work groups that were both exposed to agents that could reduce lung function to account for the disparity with Miller et al (1975) and with Lilis et al (1976).

Respiratory morbidity in PVC mixers

10. No specific studies of workers engaged on the compounding of PVC have been found, other than perhaps that by Szende, B et al (1970) who published a case report of a granulomatous lung condition in a worker engaged in shovelling PVC dust.

Respiratory morbidity and mortality in fabricators

11. Vertkin and Mamontov (1970) studying a group of 96 workers employed on PVC fabrication reported bronchitis and emphysema and impaired ventilation. X-rays also were said to show unusual changes in an unusual number of workers. They concluded that in all probability these changes were due to the action of adverse workshop environmental factors and more especially to prolonged exposure to PVC dust in high concentrations.

12. A study of mortality among PVC fabricators (Chiazze L et al, 1977) does not refer to mortality from non-malignant respiratory disease, concentrating mainly on excess neoplasms which were very likely gastro-intestinal in males and females and possibly breast and urinary organs in females. Being a proportionate mortality study the conclusions are subject to careful interpretation.

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CONCLUSIONS

13. As with many studies, it is possible to pick holes in all the reports cited above. Nevertheless, the human evidence on respiratory effects alone is sufficient to counsel prudence in exposing workers to chronic inhalation of PVC dust, even if the animal evidence (Popow, 1969; Frongia et al, 1974; Richards et al, 1975; Cylwick et al, 1972; etc.) of respiratory and systemic effects is discounted.

M GREENBERG

EMAS (E)

An additional well documented case of lung disease in a man who had worked in the bagging area of a VCM polymerization plant has been reported (Arnaud et al, 1978). X-ray changes, lung function and lung tissue changes resembled those in previous reports cited.

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APPENDIX 3

Thorax, 1978, 33, 19–25

Polyvinyl chloride pneumoconiosis[1]

A. ARNAUD, P. POMMIER DE SANTI, L. GARBE, H. PAYAN, AND J. CHARPIN

From the Clinique de Pneumo-phtisiologie, Hôpital Sainte Marguerite, Marseille and the Laboratoire d'Anatomie Pathologique, Hôpital de la Conception, Marseille, France

Arnaud, A., Pommier de Santi, P., Garbe, L., Payan, H., and Charpin, J. (1978). *Thorax*, 33, 19–25. Polyvinyl chloride pneumoconiosis. A 53-year-old man, who had been exposed for 23 years to polyvinyl chloride (PVC) in the bagging area of a vinyl chloride polymerisation plant, presented with a diffuse micronodular infiltrate on his chest radiograph. Light microscopy of lung obtained by drill biopsy showed a diffuse infiltration with histiocytes and multinucleated giant cells, with some collagen formation. Ultrastructural studies showed foreign particles in the macrophages, which were identical with PVC powder viewed under the electron microscope. Incubation of PVC powder with human lung macrophages *in vitro* showed that the macrophages engulfed the powder to give a similar ultrastructural appearance.

Pneumoconiosis due to polyvinyl chloride (PVC) was first described by Szende *et al.* (1970). Several epidemiological studies have since been made, which tend to demonstrate that PVC or vinyl chloride (VC) inhalation may be responsible for abnormalities of pulmonary function and chest radiograph (Lilis *et al.*, 1975, 1976; Miller *et al.*, 1975, Suciu *et al.*, 1975). However, histopathological descriptions of this disease are infrequent. We describe here one such case and a study of the ultrastructure of a lung biopsy specimen.

Case report

A 53-year-old man was referred in April 1974 for investigation of diffuse micronodular chest radiographic abnormalities (Fig. 1). He gave a history of chronic productive morning cough for three years, and for three months he had noticed mild weakness and slight exertional dyspnoea. He had smoked 20 cigarettes a day since age 22.

The patient had worked from November 1945 until December 1968 in the PVC bagging area of a vinyl chloride polymerisation factory. Since 1969 he had worked as a shepherd. A chest radiograph performed in 1968 as a routine factory check-up showed the same micronodular shadows. No further investigations were done. Previous chest radiographs were said to have been normal. Physical examination was negative. A scratch tuberculin skin test was weakly positive. Sputum examination for *Mycobacterium tuberculosis* on three specimens was negative.

The red blood cell count was: 4.19×10^6/l, haemoglobin 13.2 g/dl, leucocyte count 6.6×10^3/l with 40% lymphocytes and 60% neutrophils; platelets 294×10^3/l; erythrocyte sedimentation rate 6 and 20 mm/h, cholesterol 2.11 g/l; total bilirubin 6 mg/l, serum alkaline phosphatase 53 U/l; SGOT 25 U/l; SGPT 39 U/l. Pulmonary function tests showed forced vital capacity 3.82 l (expected value 5.29 l); forced expiratory volume in 1 second 2.82 l (expected value 3.89 l). Arterial blood gases: Pao_2 84 mmHg; $Paco_2$ 40 mmHg; pH 7.39. Carbon monoxide transfer factor 32.14 ml/min/mmHg (predicted value 31.75 ml/min/mmHg) (10.7 mmol/min/kPa; 10.6 mmol/min/kPa). No abnormality was seen on bronchoscopy. A lung biopsy using Steel's pneumatic trephine was performed.

LIGHT MICROSCOPY

The lung specimen was, for the most part, diffusely infiltrated by histiocytes, in which were seen a few alveolar ducts (Fig. 2). The cytoplasm of these histiocytes contained clear vacuoles. Giant multinucleated cells with vacuolated cytoplasm were also present (Fig. 3). PAS and alcian blue stains were negative. Polarised light revealed no intravascular birefringent particles. The cells were arranged in a collagen matrix, which was of thinly fibrillar aspect; a few smooth muscle fibres were also seen.

[1]Supported in part by the Institut National de la Santé et de la Recherche Médicale

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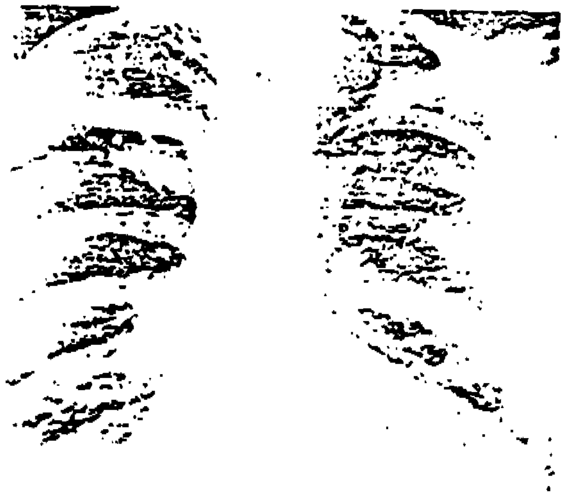

Fig. 1. Chest radiograph showing diffuse micronodular infiltrate.

Fig. 2. Lung biopsy showing diffuse infiltration with histiocytes. (Haematoxylin and eosin ×35)

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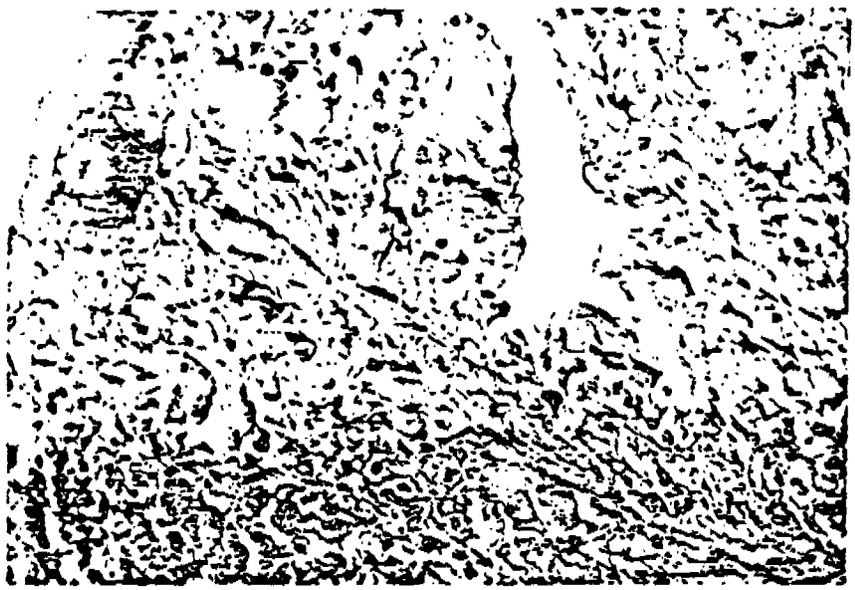

Fig. 3 *Clumps of histiocytes and some giant cells showing a finely vacuolated cytoplasm.*

ELECTRON MICROSCOPY

The specimen was fixed with 3·4% glutaraldehyde in a cacodylate buffer; post-fixation was with 2% osmium-tetroxide. The specimen was then dehydrated in acetone and embedded in Araldite. The sections were cut by a Reichert ultramicrotome, then stained with uranyl acetate and lead citrate. Examination and photographs were obtained by Philips EM 300 electronic microscope.

The cytoplasmic membrane of the macrophages had thin expansions; the nuclei were small, and chromatin was either irregularly disposed in clumps in the cytoplasm or placed against the nuclear membrane. The cytoplasm was, for the major part, infiltrated by a non-homogenous material surrounded by an electron dense membrane, whose outlines were irregular. This material was either granular or of a fluffy appearance; the granules were 0·3 to 0·4 microns in size (Figs 4 and 5). Between the phagosomes, thin cytoplasmic layers covered the organelles; the mitochondria were small in size and had well conserved cristi. The Golgi system was normal.

Electron microscopy of PVC powder

The PVC powder[1] was composed of oval grains, whose size varied from 0·5×0·3 to 1×0·3 microns. These grains were connected by PVC bridges or by the interposition of smaller granules of 0·1 micron diameter (Fig. 6).

Phagocytosis of PVC powder by alveolar macrophages

Human alveolar macrophages were obtained by bronchial lavage. About 2 to 3×10⁶ macrophages were incubated with 0·2 ml of PVC powder for 90 minutes at 37·5°C in a mixture of 20% of compound 199[2] and 80% of fetal calf serum[2]. The macrophages were then treated and examined with the electron microscope according to the method previously described. The absorption of the PVC particles in the cytoplasm of these cells was rapidly accomplished. The particles appeared in the phagosomes as either oval corpuscules or clusters which were variable in size (Figs 7 and 8). At this stage, the particles showed no evidence of degradation. Thinly granular lysosomal material was deposited against them. The cytoplasm of the macrophages contained mitochondria, bundles of microfilaments, and multiple lysosomes.

Discussion

In this case of discrete pulmonary fibrosis associ-

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Fig. 4 *Histiocyte with a small eccentric nucleus (N); the cytoplasm is mostly occupied by irregularly outlined phagosomes containing a fluffy granular substance. Collagen fibres (C). (EM ×13 900)*

Fig. 5 *Biopsy specimen; fluffy material with irregular outlines surrounded by a dense membrane (=). Phagosomes are confluent in places (—). (EM ×37 000)*

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Fig. 6 PVC powder made of oval submits of variable size; they are linked together by smaller particles (—). (EM ×46 000)

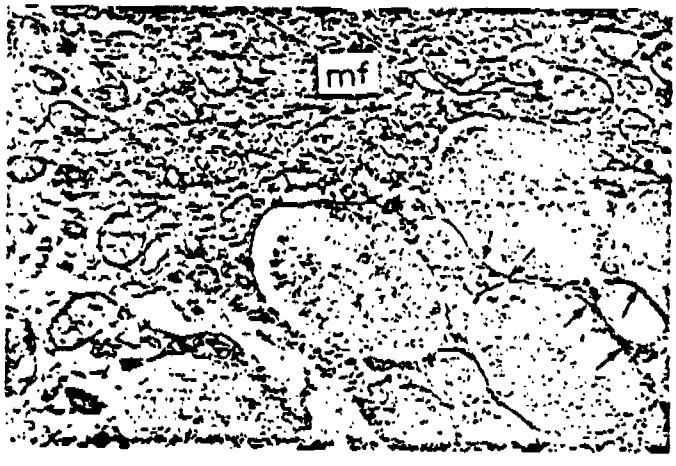

Fig. 7 In-vitro study of PVC particle phagocytosis by an alveolar macrophage showing oval bodies of uneven size with irregular outline, sometimes surrounded by finely granular lysosomal material (—); microfilaments (m F). (EM ×37 000)

ated with a granulomatous reaction the lesions contained particles which could not be identified by the usual stains. We suggest that this may be pneumoconiosis induced by PVC inhalation.

The chest radiographic abnormalities in our patients are the same as those described by Lilis *et al.* (1975); these authors showed that 48·6% of workers exposed in their work to PVC dust for at least 20 years have reticular and/or micronodular chest radiographic shadows. The histological lesions we describe are identical with those recorded by Szende *et al.* (1970), who reported the case of a 31-year-old man who had worked for 12 months in an environment containing high levels of PVC. This patient had severe respiratory failure. Pulmonary biopsy showed diffuse fibrosis associated with focal granulomatous lesions whose cells contained ovoid or polygonal particles. These lesions are the same as those experimentally provoked by Frongia *et al.* (1974), who exposed guinea-pigs and rats from two to seven months in a room where PVC powder was bagged. Examination of the guinea-pigs showed an earlier reaction at alveolar level composed of macrophages and giant multinucleated cells. These cells contained minute intracytoplasmic granules, which were not stained by the usual methods. On later examination, these lesions became focal granulo-

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Fig. 8 *In-vitro study of an alveolar macrophage in contact with PVC for 90 minutes. Particles of PVC are accumulated in a phagosome, which occupies almost all of the cytoplasm (...). Smaller phagosomes engulf oval corpuscules and small granules of PVC. (EM ×6800)*

mas. Examination of rats showed more pronounced initial fibrotic lesions but later lesions were comparable with those observed in the guinea-pigs.

The identical morphology of the intracellular foreign particles observed in our patient, and the microscopic appearances of the PVC powder and of the inclusions in human macrophages which have engulfed PVC powder *in vitro*, are convincing evidence that our case can be considered to be that of PVC pneumoconiosis.

Clinically, the evolution of PVC pneumoconiosis is uncertain. Our patient had only a slight reduction in vital capacity with no reduction in gas transfer factor, suggesting that the fibrosis was not as yet of much functional significance; on the other hand, Szende and co-workers (1970) reported a case with severe respiratory impairment. Occupational exposure to PVC dust may have been different in these two cases. Our patient was exposed to PVC dust only, while Lilis *et al* (1975, 1976) showed that PVC dust inhalation induced less severe respiratory function abnormalities than simultaneous inhalation of vinyl chloride monomer and PVC. This must be compared with the results described by Prodan *et al* (1975), who showed that, in the guinea-pig, two hours' inhalation each day of air containing 10% vinyl chloride monomer over two weeks could produce diffuse pulmonary fibrosis. Further studies of the mechanisms of this pneumoconiosis are in progress.

We thank Dr. Allan Towne and Dr. Christian Capo for their help.

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SYNTHESIS OF THE RESULTS OF THE EPIDEMIOLOGICAL INVESTIGATION CARRIED OUT IN ITALY ON WORKERS EXPOSED TO VCM

Summary

The investigation has started on the first days of 1975 and involved approx.two years of work.

Plants concerned :

- Porto Marghera	MONTEDISON	
- Brindisi	MONTEDISON	
- Terni	MONTEDISON	
- Ravenna	ANIC	
- Ferrara	SOLVAY	
- Rosignano	SOLVAY	
- Ferrandina	LIQUICHIMICA	
- Cagliari	SIR RUMIANCA	
- Porto Torres	SIR RUMIANCA	
- Bollate	MONTEDISON	(pilot-plant)
- Villadossola	MONTEDISON	(pilot-plant)
- Borgaro Torinese	SIR	(pilot-plant)

It has been considered "exposed" all the workers living or dead, exposed presently or in the past to vinyl chloride for a minimum period of six months.

The investigation has been carried out on 4713 workers, equal to 81% of the exposed ones. It has been possible to ascertain the death of 64 workers, but it is not sure that it is a question of the totality of the deaths which happened in workers exposed during the period taken into due consideration (from starting of production of VCM up to 1975).

Synthesis

Employeers	presently exposed	3.071
Employeers	ex exposed	1.239
Contract Work	presently exposed	314
Contract Work	ex exposed	36
Uncodified		3
	Total	4.713
Dead		64
	Total	4.787

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Taking into account the fact that "time of exposure" and "level of exposure" change, we have been able to calculate an index of exposure and consequently divide the workers into three exposure classes to be considered indicative.

Synthesis	Exposure Class			
	low	average	high	uncalculated
N° of workers	1.058	2.436	1.107	70

Clinical instrumental and laboratory investigations

Lung:	X-ray photograph of the chest - cytological examination of expectoration
Hands:	X-ray photograph of hands - photopletismographic of the ten fingers in basis conditions and after cold test
Liver:	SGOT and SGPT - gamma GT - alkaline phosphatase - bilirubinemia
Urine:	complet examination + cytological examination of sediment in case of hematuria
Blood:	complet hemocromocytometric examination - calculation of platelets
Endothelium:	study of the vascular centre of eye bottom

The above information has been recorded in an epidemiological filing-card.

RESULTS

X-ray photograph of the chest

Stressing of the bronchial filling	28 %
Report "compatible" with neoplasia	2 cases (in one confirmed
Results tbc	5,7 %
Others	3 %

In the single classes of age the frequency of report" stressing of the filling" increases with time of exposure.

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It has been noted, in workers in sorking, drying up and stores, 23 cases of pneumoconiosis in workers, which surely have had no further exposures to organic or inorganic dusts.

Cytology of spitting

No significant fact has been shown.

X-ray photograph of hands

Normal	4.000
Results from fractures	165
Suspected acrostheolisis	~~137~~
Certain acrostheolisis	27

Photopletismographic examination

3.977 workers have followed the basis tracing and 3.866 did the tracing after cold test.

During the basis tracing 150 cases showed pathological modifications and 742 did the same during the cold test.

96 workers (2,5%) showed pathological modifications of the basis tracing as well as of that after cold test; their distribution in different classes showed that frequency of contemporaneous pathological modification of the two tracings increases in accordance with the increased exposure, quantified by index as well as by time.

Examination of the eye bottom

This examination has been carried out on 4.066 workers. The more significant results are as follows :

sclerosis	488
hemorrhages	14
crossing	63

Insofar sclerosis regards, there is no correspondence between frequency of report and index of exposure.

Vascular syndrome

Among the 3.212 workers submitted to X-ray photograph examination of hands, photopletismographic examination and of eye bottom, four workers (0,12%) showed contemporaneous pathological modification of the three examinations.

These cases can be referred in some manner to a "syndrome of vascular type".

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Hematology

No significant findinds concerning RBC, hemoglobin and WBC have been noted.

It has been noted 339 cases (7,5%) of thrombocitopenia in statistically significant progression with increase of exposure.

Analysis of urine

Normal	3.822	83 %
Hematuria	237	5,2 %
Albuminuria	266	5,8 %
Hematuria + Albuminuria	22	0,5 %
Glycosuria	68	1,5 %
Urobilinuria	182	40 %

The frequency of the microhematuria resulted in relation with the index of exposure.

Liver functions

The more frequent pathological changes are the increase of the gamma GT in 28,3% of cases and the presence of hepatomegalia in 44,5% of cases.

Among whom in which an important hepatomegalia is noted, there are more frequent also the thrombocytopenia, acrosteolisis or the patologic photopletismographic value: consequently a syndrome due to vinyl chloride is to be supposed.

Mortality

Cause of death	n°	partial total	Total
Infarct myocardium	9		
Other cardiopathies	1		
Encephalonvasculopathy	6	16	
Tumours			
Trachea	1		
Lung	6		
Lachrymal sac	1		
Esophagus	2		
Stomach	1		
Encephalon	1		
Bladder	3		
Liver	4		

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Hepatic angiosarcoma	3		
Adenocarcinoma cholecysts	1		
Peritonaeum	1		
Cutaneous	1		
Testes	1		
Leukemia	2		
Hodgkin	2	30	
Chronic aggressive hepatopathy	5		
Renal failure	3		
Other causes	8	16	
Not taken into due consideration (Terni plant)	2	2	64

It appears from the above that among workers exposed to vinyl chloride the cause of death "tumour" is quite more representative if compared with the expectations.

FM/lu
20th Febr.1978

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