

VCM

Tip of the iceberg?

Our medical correspondent writes: Recent reports of liver cancers in men who have been heavily exposed to vinyl chloride monomer (vcm) could well change attitudes towards the need for testing industrial chemicals for carcinogenicity as dramatically as the thalidomide tragedy changed attitudes on testing prospective drugs for teratogenic activity. Many toxicologists will welcome such a change, which they feel to be long overdue.

The story as far as cancer risk is concerned should have begun in 1971 with a report from an Italian laboratory published in *Cancer Research*, a widely read cancer journal, that 17 out of 25 rats exposed to 30 000 ppm of vcm for 20 hours per week developed cancers of the acoustic duct, bones and other sites. Perhaps because laboratory workers cry wolf rather too often, little notice was apparently taken of the 1971 report except that confirmatory experiments were undertaken in other laboratories with positive results. So it has taken the tragedy of deaths of humans from an otherwise rare form of cancer of the liver—angiosarcoma—to bring the dangers of exposure to vcm to the surface of public awareness. And now that, in 1974, we can all see what may be the tip of an iceberg above the surface, a flood of questions comes to mind. For each case of vcm liver cancer that we know about, how many new cases have there been, or will there be? All the known cases were in men very heavily exposed to vcm. Does less exposure carry proportionately less risk, or is there a threshold below which exposure carries no risk? Is the risk of developing cancers of other kinds increased by exposure to vcm? Does contamination of food with vcm escaping from pvc used for wrapping purposes constitute a hazard? Is contamination of the atmosphere with vcm liberated when pvc is heated dangerous for man? Are other intermediates used in the manufacture of plastics carcinogenic?

Prior to the *Cancer Research* report it was widely held on the basis of animal studies that vcm is without toxic effect other than temporary narcosis. However, in humans it has been recognized since 1957 that exposure to vcm is associated with a progressive disease of the skin and bones with symptoms of vascular disturbance affecting the extremities (Raynaud's phenomenon). This package of signs and symptoms, which did not include cancer, became known as 'acro-osteolitis' or 'vinylchloride disease' (vcd). More recently it has become apparent that the manifestations of vcd include evidence of chronic liver intoxication with obstruction of blood flow leading to dilatation of, and bleeding from, oesophageal veins and to enlargement of the spleen. The men most heavily exposed to vcm are those responsible for cleaning autoclaves used in the manufacture of pvc. The immediate effects of exposure are disorientation,

drowsiness, fatigue and interference with blood coagulation, and it is of anecdotal if no other interest that vcm was once assessed for its possible value as an anaesthetic. It is among autoclave cleaners in pvc manufacturing plants that the first, and so far only, cases of liver cancer have been seen. Such men may be exposed to atmospheres containing more than 1000 ppm vcm. No case of liver cancer has been found in anyone exposed to vcm for less than 15 years.

Usual features of exposure to carcinogens are a long interval between the start of exposure and the onset of disease, and the risk of cancer development continuing long after exposure ceases. The fear that the few cases of vcm cancer so far seen may herald a more extensive outbreak of the disease stems from a consideration of these two features. That no cases of vcm cancer have yet been seen in persons less exposed to vcm than autoclave cleaners may also be deceptive, since induction time tends to be inversely related to exposure dose. In theory there is no basis for confidently expecting a threshold level below which exposure to vcm will carry no cancer risk, and no assurance that a level of exposure that causes no immediate ill effects is carcinogenically safe.

However, the issues at stake are manifestly practical ones which should not, and will not, be determined solely on the basis of theoretical consideration. In the short term we cannot envisage life without pvc, nor can we be sure that the manufacture of other plastics is without comparable but as yet unknown health risks to workers. Panic measures are not indicated. However, manufacturers should certainly redouble their efforts to protect workers from exposure to vcm, processes should be further enclosed, and the job of autoclave cleaner should be abolished. Safety Officers, while not forgetting the fire and explosion hazards involved in handling vcm, must in future take long-term health hazards to workers at least as seriously. Threshold limit values which were reduced from 500 ppm to 200 ppm in the light of evidence of a possible effect on liver function in men exposed to vcm should be both brought down to very much lower levels and more rigorously enforced with the aid of effective monitoring. Workers who have already been extensively exposed to vcm, especially those who have signs of acro-osteolitis, should be moved to other work immediately, and those who continue to be exposed at any level should be subjected to regular health checks and removed from the work if signs of exposure, e.g. thrombocytopenia, are found.

We cannot yet know the full extent of the iceberg of which we may now only be seeing a tip. In general, the response of laboratory animals to carcinogens is clearly dose-related and experience in humans exposed to carcinogenic agents such as asbestos suggest that the vast majority of men exposed at work to doses of vcm materially below those received by autoclave cleaners will not develop cancer because of that exposure. Even

the risk among autoclave cleaners may not be high. Idiosyncrasy may have been a factor in determining the occurrence of cancer in the known cases.

We do need more hard factual information about possible contamination of food or the atmosphere with vcm derived from pvc. Meanwhile, common sense indicates that exposure of ordinary people to vcm in this way must be several orders of magnitude less than that of the least exposed workers in a pvc manufacturing plant. If the extent of contamination of food and the atmosphere can be reduced below present levels this should be done, but there is certainly no cause for real concern on this score at the present time. Vcm has in the past been used in some countries as a propellant for hairsprays. Obviously this kind of use must now be regarded as completely unacceptable on health grounds.

It is clear that the industry, Governments and Trade Unions concerned are

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Services rendered

Photographic collection of intensity data may be inherently inferior to electronic measurements on a diffractometer but photography does have the advantage that very many reflections are recorded simultaneously. Besides, photography is cheap. The tedium and the relatively poor quality of typical photographic intensity data is mostly due to the difficulties of visual estimation of the spots on the films. Could this not be automated?

Crystallographers using photographic methods will recall that the Science Research Council circulated a questionnaire about three years ago to assess the demand for a central service providing automatic densitometer measurement of diffraction intensities on films, especially Weissenberg films. The response was encouraging. A steering panel for the project was set up; an Optronics automatic scanning microdensitometer was purchased and installed at the Atlas laboratory at Chilton and, with the appointment of Dr Mike Elder to the project, work started on the development of the necessary computer programs. Programming the densitometry of Weissenberg films proved a difficult task, particularly as no satisfactory programs of any kind had been set up for this kind of photograph. However, success has been achieved. The equipment and its associated software is now able to index reflections and measure their integrated intensities on Weissenberg films, achieving precision definitely better than visual estimates and, of course, much greater speed.

UK structural crystallographers interested in making use of this new service should write to Dr M. Elder, Atlas Laboratory, Chilton, Didcot, Berks, for further information.

treating the situation regarding vcm toxicity for man both very seriously and as a matter of urgency. Harold Walker, Parliamentary Under-Secretary at the Department of Employment, announced on 17 May that the Chief Inspector of Factories had invited TUC and CBI participation in discussions to prepare a code of practice. 'It would be sensible to adopt as an interim standard a ceiling value of 50 ppm and a time-weighted average of 25 ppm, allowing that wherever practicable exposures should be brought as nearly as possible to zero concentrations, he said. Other considerations would be systems of monitoring and medical supervision.

UK companies—the decent thing

£4m is to be spent by the four UK pvc polymerization companies (ICI, BP, Vinatex and British Industrial Plastics) on reducing average vcm concentrations in plant atmospheres. The money will go on automated cleaning of autoclaves, improved ventilation systems and modification or checking of joints, valves and so on. At the moment industry reckons that average exposure levels are around 50 ppm; A. W. Barnes, chairman of the Chemical Industries Association's Vinyl Chloride Committee, confidently expects that levels will be cut by half by the end of the year, and subsequently (but over no rigid time limit) be reduced to 10 ppm. This level would be the ultimate for most existing plants, and possibly out of reach for older ones. According to the CIA 'Entirely new plants with the most modern technology might achieve 5 ppm. Figures below this are not conceivable'. And even though the committee believes that 'the residual risk is very small, if it exists at all', the only certain way of reducing the risk to zero would be to stop pvc production—and pvc is an essential material used in domestic and industrial buildings, packaging, gramophone records, footwear and the mining and motor industries.

Since the January announcements the UK chemical industry, no doubt conscious of its poor image, has been making considerable efforts to be seen to be doing the right thing. The companies first informed Dr Robert Murray, TUC medical adviser, and then held meetings with workers at all the factories concerned—'excellent cooperation' has been shown by the unions. All relevant government departments were immediately contacted, the Factory Inspectorate being 'very heavily involved', and a Vinyl Chloride Committee was set up under the auspices of the CIA 'within a couple of weeks'. But there are still at least two disconcerting facts. First, it was only because of the extreme rarity of angiosarcoma that the hazard was detected; if lung cancer had been caused it seems that no-one would have been the wiser. And second, even if attitudes towards testing new industrial chemicals for carcinogenicity change, will other unsaturated monomers now used by the industry—such as styrene—be subjected to the stringent tests that are so obviously necessary?

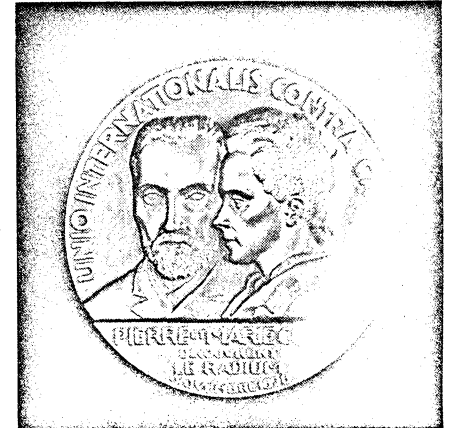
Royal Society

Science at night

'A *soirée* or other assembly of an intellectual character, in connexion with literature, art or science', seems to be the most general of the three definitions of 'Conversazione' offered by the *Shorter Oxford English Dictionary*. The one held by the Royal Society mainly confines itself to the last of the three categories, although medals of science, as exhibited by Dr A. R. Michaelis at this year's event, are often of great value as works of art. The 27 exhibits covered the entire range of science; chemistry was featured in the use of Auger electron spectroscopy in analysing fracture surfaces and corrosion products, while a team from the Research Laboratory of the British Museum demonstrated 'Chemistry in conservation'—the consolidation of waterlogged wood and the cleaning of Egyptian limestone sculptures. Four workers from the Wolfson Institute of Interfacial Technology, Nottingham University, displayed fibre-reinforced materials with self-adjusting interfaces; under overload conditions the fibre/matrix interface decouples and loads can be transferred

to remote parts of the composite structure. Much greater amounts of energy can therefore be absorbed; cracks propagate far less easily than in conventional materials. Dr I. J. Graham-Bryce and colleagues from Rothamsted Experimental Station showed the use of pheromones in pest control, while the Vapipe from Shell Research (the only industrial company featured) and the National Engineering Laboratory reduces fuel consumption and exhaust emissions from car engines. Heat from the exhaust gases is used to vaporize the fuel in the inlet tract, giving a homogenous air-fuel mixture; this allows a much leaner mixture to be used.

Altogether a most interesting selection, even if lacking in industrial content; and being chosen to exhibit is considered quite an honour. But a great deal of trouble and expense is involved just to provide Fellows and invited guests (wives are not allowed, but Lady Guests are) with an evening's entertainment and to give 300-odd children a morning away from lessons the next day. This was emphasized by another *soirée* on 27 June—to which wives were allowed—which featured almost exactly the same exhibits; it would be a lot more sensible to let the ladies into the first one even if tradition is flouted.



Above: Science medals from Dr A. R. Michaelis' private collection. (Photos: Ronan Picture Library)

Below: Waterlogged alder wood, air dried without treatment. Most cells have collapsed.

(Photo: by permission of the Trustees of the British Museum)

