2B

VISIT TO ROSIGNANO SOLVAY

14 - 15 OCTOBER 1974

As a consequence of Professor Viola's visit to Runcorn, where he presented data from an experiment on the carcinogenicity of vinylidene chloride to a DOW/ICI meeting on chlorinated solvents, I decided to visit his laboratory to obtain as much detailed information as possible. This was essential, in my opinion, because action arising out of the discovery of the carcinogenicity of vinylidene dichloride could be seriously misdirected if the basic experimental information were incorrect.

The following information was obtained by first hand observation:-

Sections from 15 animals were examined. Slides were numbered

1 (a) Lymph gland and selivary gland - normal
(b) Subcutaneous tissue from area adjacent to the ear - abscessation
(c) Liver - normal
(d) Lung - lymphoid hyperplasia especially in the peri-bronchial region
(e) Sub-cutaneous tissue - large abscess with active granulation tissue

3 (a) Lymph gland, intra-abdominal marked autolysis, pycnosis and polymorphonuclear leucocytic infiltration. Some large cells with vesicular nuclei left attached to remnants of trabecular tissue. The diagnosis is very difficult because of autolysis and the absence of other tissues from this animal. This may be a reticulum cell sarcoma or could represent autolytic changes in hyperplastic lymphoid tissue. This section is available at CTL.

4 (a) Lymph gland. Professor Viola called it No 3 but it was marked 4. Very similar to 3.

5 (a) Subcutaneous tissue adjacent to the ear. Massive abscessation and lymphoid reaction.

6 (a) as for 5 (a)

7 (a) "

8 (a) "

9 (a) Lung. Heavy deposits of formalin pigment. Normal.

(b) Subcutaneous tissue (?)

Abscess with massive infiltration of polymorphs in surrounding connective tissue. A few large cells with large pale nuclei, frequently multilobbed. No signs of infiltration and a low mitotic index. Not considered a tumour.

10(a) Subcutaneous tissue. Abscess and cellulitis.

(b) Spleen. Large cells present similar to those in lymph gland from animal 3. Many cells with lobulated nuclei. Autolysis advanced making a positive diagnosis very difficult. If it is a tumour it seems more likely to be from the myeloid series. In my opinion it is not a tumour.

11(a) Liver. The PM form described a large liver tumour. In this section a small focus of infiltrating spindle cells.

(b) Lung. Massive metastatic tumour with spread to diaphragm and lung. A malignant tumour is definitely present. Diagnosis of spindle cell sarcoma as differentiation into leimyo sarcoma, fibrosarcoma etc impossible on material available.

12(a) An abdominal mass. Large abscess with muscle fibres in the capsule. Many polymorph nuclear leucocytes in abscess and surrounding tissue. No mitoses. Probably an abscess surrounded by active granulation tissue.

(b) similar to (a).

20 (a) Liver. Infarct.

22 (a) Liver. Midzonal necrosis.
Signs of early fibrosis.

33 (a) Large intra-abdominal mass.
The cells are pleomorphic and spindle shaped. Low mitotic index. Nucleus vesicular and pale. Some multinucleate cells. In this are a number of ducts lined with a low cuboidal epithelium with basophilic cells. The site of origin uncertain but is probably abdominal wall of a female rat with mammary gland. Probably an abscess.

42 (a) Mass attached to intestine. Spindle shaped pleomorphic cells
Spindle cell sarcoma.

On further discussion it was evident that these were the total of all tumour bearing animals in his VDC experiment. He had no H/E forms or sections from the remaining animals nor from his control group. His control group was identical with that used for the VC experiment and the VDC animals were descendants of the same breeding animals. No tumours were observed in the controls.

Thus the experiment apparently consisted of:-

37 ♀ and 37 ♂ rats of a Wistar derived strain.

Exposed 4 hours/day, 5 days/week for 9 months (6 months at 200 ppm and then 3 months at 100 ppm).

80% of animals were alive at 10 months. Most died 12 - 15 months from start and the last died at 18 months. The earliest 'tumour' was observed at 10 months.

The compound used was $H_2C = \underset{Cl}{\overset{Cl}{C}}$

Professor Viola asked me to edit the paper for presentation at Florence. There were a number of minor alterations to the VC report. With little persuasion he changed the VDC report's first sentence from 'Experiments on another chemical, vinylidene chloride monomer, show that it is strongly carcinogenic .....' to 'Preliminary experiments on another chemical, vinylidene chloride monomer, indicate that it may have carcinogenic activity in experiments similar to those described above .....'.

Conclusion: In my opinion there is insufficient evidence available from this experiment to draw either positive or negative conclusions about the carcinogenicity of vinylidene dichloride. Current experiments on VDC e.g. those being carried out at DOW should be reviewed to ensure that the dosage given to the rats is equivalent to that used by Solvay. A negative result from lowere dosage will be insufficient to convince regulatory authorities. Epidemiology should await a more definite diagnosis of tumour type.