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Suitable Models for Long-Term Bioassays of Therapeutic and Toxic Effects of Antiblastic Drugs: Brain Tumours of Neuronal Cells and Primitive Bipotential Precursors Produced in Sprague-Dawley Rats by Vinyl Chloride

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At present, very little is known about the chemotherapy of brain tumours of neuronal cells and of their primitive bipotential precursors, i. e., of medulloepitheliomas, medulloblastomas and neuroblastomas. A suitable experimental model, providing an animal equivalent to the human situation, would be a useful tool to improve our knowledge in this field.

It has been shown in our Institute that exposure by inhalation to vinyl chloride, at doses varying from 2,500 to 10,000 ppm, can induce tumours of neuronal cells and of their precursors in Sprague-Dawley and Wistar rats (Maltoni and Lefemine, 1975; Maltoni, 1977; Maltoni et al, 1980). In this report we describe experimental means of inducing a high incidence of these tumours over a relatively short period, and therefore of making available a sufficient number of these tumours for testing antiblastic drugs.

Sprague-Dawley rats were exposed by inhalation to 2,500 ppm of the monomer from the 12th day of embryonal development to one year of age: Breeders were exposed 4 hours daily, from the 13th day of pregnancy to delivery; offspring were exposed 4 hours daily, 5 days weekly, for 5 weeks, and then 7 hours daily, 5 days weekly, for 50 weeks.

The incidence and the latency of the tumours obtained are shown in Table 1. Microscopically, the tumours displayed different potentialities, which varied from tumour to tumour and in different areas of the same tumour, and which represent the equi-

Table 1.
Incidence of brain tumours of neuronal cells and primitive bipotential precursors in Sprague-Dawley rats exposed from 12-day embryonal life for 57 weeks to vinyl chloride in air at 2,500 ppm, 4—7 hours daily, 5 days weekly

Animals used			Animals with brain tumours		
Sex	No. at start	Corrected no.[a]	No.	%[b]	Average latency (weeks)[c]
M	63	57	27	47.4	45.5
F	65	57	28	49.1	48.4
M and F	128	114	55	48.2	47.0

[a] Animals alive at 35 weeks, when the first tumour was observed
[b] with respect to the corrected number
[c] From start of treatment

Fig. 1

Fig. 2

Fig. 1. Medulloepithelioma in Sprague-Dawley rat, following exposure to vinyl chloride by inhalation. H.-E. × 80.

Fig. 2. A detail of Figure 1. × 130.

Fig. 3

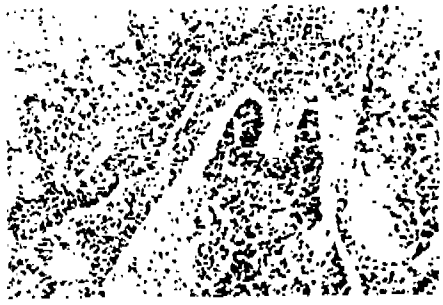

Fig. 4

Fig. 3. A detail of Figures 1 and 2. × 200.

Fig. 4. A detail of Figure 1. × 200.

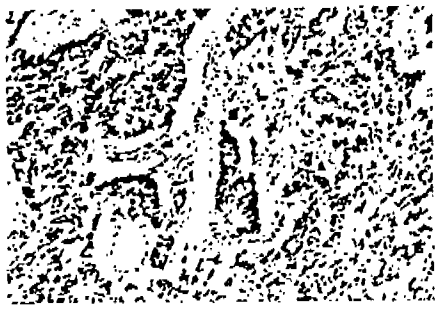

Fig. 5

Fig. 6

Fig. 5. Medulloepithelioma in Sprague-Dawley rat, following exposure to vinyl chloride by inhalation. H.-E. × 200.

Fig. 6. Medulloblastoma in Sprague-Dawley rat, following exposure to vinyl chloride by inhalation. H.-E. × 200.

Fig. 7

Fig. 8

Fig. 7. Medulloblastoma in Sprague-Dawley rat, following exposure to vinyl chloride by inhalation. H.-E. × 200.

Fig. 8. Medulloblastoma in Sprague-Dawley rat, following exposure to vinyl chloride by inhalation. H.-E. × 320.

valent of the human medulloepithelioma, medulloblastoma and neuroblastoma. Typical pictures are shown in Figures 1—8.

It is of particular interest for the testing of drugs that these tumours manifest themselves with characteristic symptoms several days before the death of the animal. The major symptoms are a reduction in muscle tone, hypomotility, ruffling of hair. reduction in food intake, loss of body weight and exophthalmia.

References

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