

The Production of Tumors in Rats by the Implantation of Pure Polyethylene*

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This report confirms the production of tumors in rats by pure polyethylene implanted in the abdominal wall, and, in addition, the production of tumors by the implantation of polyethylene over the skull is described.

Oppenheimer *et al.* (1-3) have reported the production of malignant tumors in rats by the implantation of various plastics in the abdominal wall. The frequency of tumor production varied from 4 per cent to 45 per cent, depending upon the plastic used. Among these plastics were two types of polyethylene: one of a commercial grade and one considered to be pure. They found that the pure polyethylene without a plasticizer induced tumors in 18 per cent of the rats. These tumors were chiefly fibrosarcomas and could be transferred through several generations in rats.

Since polyethylene is used for many surgical procedures and is often left in the tissues, confirmation of these observations is important even though the relationship between the production of tumors in rodents and the production of tumors in man is not known.

MATERIALS AND METHODS

Pure polyethylene film¹ of the kind used in clinical procedures was employed as the test substance. This was washed with detergent, rinsed with water, heat-sealed in polyethylene sacs (same material), and sterilized with high voltage cathode rays.

Two strains of rats were used, namely, Wistar and Hisaw (originally from Wistar stock). There were equal numbers of each sex. Fifty rats of each strain had polyethylene aseptically implanted subcutaneously in the abdominal wall and subgaleally

over cranial defects. The pieces of polyethylene were square, about 1.5-2 cm. on each side. Fifty additional rats (Hisaw) were used as a control group. These animals were subjected to an identical surgical procedure, but no polyethylene was imbedded. All these rats were then allowed to live until they developed tumors or died. All were kept in the same room and fed the same diet.

RESULTS

Of the original 150 rats, 59 were lost in their cages by cannibalism, and another six died soon after implantation of the plastic and would not be expected to have developed a tumor. Thus, there were 85 rats that survived long enough to develop tumors and were observed until they died or were sacrificed; 28 of these were controls, and 63 had polyethylene implants. The survival times of the 28 control rats were: 8-12 months, 22; 12-18 months, 14; 18-25 months, 6. The survival times of the 63 rats with polyethylene implants were: 8-12 months, 61; 12-18 months, 49; 18-25 months, 30. All surviving animals were sacrificed 25 months after the implantations.

Sixteen tumors developed in the 63 rats with polyethylene implants. Eight were associated with polyethylene implants and had the appearance of fibrosarcoma. Seven were breast tumors of various types, in females, unassociated with polyethylene; and one was a hepatoma, in a male, also not associated with polyethylene.

The eight tumors associated with the polyethylene implants were equally distributed between the males and females. Six of these tumors were associated with the abdominal polyethylene implants and two with the cranial polyethylene implants. The first tumor associated with polyethylene became apparent a year and 2 months (434 days) after implantation of the polyethylene over a cranial defect. The second tumor, associated with an abdominal polyethylene implantation, appeared after a year and 4 months (479 days). The

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¹ Procured from Clay Adams, Inc., 141 E. 25th St., New York 10, N.Y.

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remaining tumors were first observed at 633, 672, 691, 738, 740, and 738 days.

In the control group five tumors developed. All were in females: four were breast tumors and one a carcinoma of the bowel. None of these was related to the operative sites.

In summary (Table 1), there was a 12.7 per cent incidence of tumors associated with the polyethylene implants, and none in the controls. There was a 21 per cent incidence of breast tumors in the female rats with polyethylene implants and a 29 per

cent incidence of breast tumors in the females of the control group.

Thus, it is probably the polyethylene alone which causes the tumors. The latent period observed in these experiments was slightly longer than that observed by Oppenheimer *et al.*, but the difference is not significant in terms of the data available. This long latent period, which allows the rat to survive until old age, raises the possibility that there may be some factor associated with aging which is in some way responsible for the tumor formation. If there is an aging factor, it could be a species effect. Further

TABLE 1
TUMORS FOUND IN RATS WITH PURE POLYETHYLENE IMBEDDED IN
THE ABDOMINAL WALL AND IN THE SKULL

STRAIN	SEX	No. RATS	RATS WITH POLYETHYLENE IMPLANTS Fibrosarcoma associated with plastic		Other tumors		No. rats	CONTROL OPERATION WITHOUT POLYETHYLENE Fibrosarcoma or other tu- mors at opera- tion site		Other tumors	
			Abdomen	Skull	Breast	Other		Breast	Other		
Hisaw	F	20	3	1	5	0	14	0	4	1	
Hisaw	M	17	3	0	0	0	14	0	0	0	
Wistar	F	13	0	1	2	0					
Wistar	M	13	0	0	0	1					
Total:		63	6	2	7	1	28	0	4	1	
Frequency:			12.7 per cent		21 per cent (females only)			29 per cent (females only)			

cent incidence of breast tumors in the females of the control group.

Although there is some difference in the incidence of tumors between the two strains, the numbers are small and probably do not indicate a true difference. This is supported by the fact that the Oppenheimer group used the Wistar strain in their experiments.

COMMENTS

These results confirm the observations of Oppenheimer *et al.* (1-3) that polyethylene implants in rats excite the formation of tumors resembling fibrosarcoma. The incidence of 12.7 per cent found in this study is in good agreement with the 12-18 per cent incidence reported by Oppenheimer for various polyethylene implants.

The effect of the polyethylene seems to be only local. The presence of the implants did not change the incidence of spontaneously appearing breast tumors in the female rats.

This effect cannot be ascribed to a plasticizing agent, since the pure polyethylene used in these experiments had none. The operations in which no plastic was implanted in the control group appear to eliminate possible nonspecific surgical factors.

experimentation will be required to settle this point.

SUMMARY

1. A 12.7 per cent incidence of fibrosarcoma was found in rats with polyethylene implants. No tumors were found in a control group which received similar surgical treatment but in which no polyethylene implant was made.

2. Sex was not a factor in the production of tumors by polyethylene.

3. The tumors occurred both with implants in the abdominal wall and over the skull.

4. The polyethylene implants did not affect the incidence of breast tumors in females.

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