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SARCOMAS AT THE SITE OF IMPLANTATION OF A POLYVINYL PLASTIC SPONGE: INCIDENCE REDUCED BY USE OF THIN IMPLANTS

F. J. C. ROE, C. E. DUKES and B. C. V. MITCHLEY

Chester Beatty Research Institute,
Institute of Cancer Research: Royal Cancer Hospital, London, S.W.3

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Abstract—1. Nine out of 24 CB stock rats bearing 20 × 20 × 5 mm (2000 mm³) subcutaneous implants of polyvinyl sponge developed local sarcomas, whereas only one out of twenty-four bearing 33 × 33 × 2 mm (2000 mm³) implants did so.

2. Five sarcomas arose in twenty-four rats bearing 12·6 × 12·6 × 5 mm (800 mm³) implants, and only one out of twenty-four bearing 20 × 20 × 2 mm (800 mm³) implants did so.

3. The incidence of sarcomas in inbred Woodruff Hooded rats in response to 20 × 20 × 5 mm implants was similar to that in CB stock rats.

4. It is concluded that local tumour induction is dependent on the thickness of the sponge implant and not primarily on the amount implanted.

5. These findings suggest that, as far as possible, the implantation of thick pieces of polyvinyl sponge should be avoided in human surgery.

DUKES AND MITCHLEY[1] reported a high incidence of sarcomas at the site of implantation of 20 × 20 × 5 mm pieces of polyvinyl sponge into the subcutaneous tissues of male Chester Beatty stock albino rats. All of fourteen rats which lived for 10 months or more developed sarcomas. On the other hand, only one out of eighteen survivors at 10 months developed a sarcoma in response to the subcutaneous implantation of 20 × 20 × 2 mm pieces of sponge. The highly significant difference in incidence of sarcomas between the two groups was thought to be attributable to the difference in thickness of the pieces implanted. However, it was necessary to check this experimentally because apart from the difference in thickness there was also a 2½-fold difference in "dose" of sponge. The experiment described below confirms that thickness and not dose of sponge is the important determinant.

It was also desirable to see whether the induction of sarcoma by polyvinyl sponge was a strain-specific phenomenon. For this purpose pieces of sponge were implanted subcutaneously into rats of a second strain.

EXPERIMENTAL DETAILS

Pieces of polyvinyl plastic sponge (Trade name "Prosthex", made by Ramer Chemical Co., Camberley, Surrey) were cut to size, sterilized by boiling in distilled water for 20 min and implanted into five groups of twenty-four 8-week old male Chester Beatty stock albino rats as follows: *Group 1*–20 × 20 × 5 mm (volume = 2000 mm³); *Group 2*–20 × 20 × 2 mm (800 mm³); *Group 3*–12·6 × 12·6 × 5 mm (800 m³); *Group 4*–33 × 33 × 2 mm (2000 mm³); *Group 5*–8 × 8 × 5 mm (320 mm³).

Pieces were implanted into the subcutaneous tissues of the right flank through an incision in the skin made under ether anaesthesia. In addition, 20 × 20 × 5 mm pieces were similarly implanted into twenty-four 8-week-old male rats of an inbred black and white hooded strain (obtained from Professor Woodruff, Edinburgh).

After operation the animals were housed eight per cage in metal boxes, fed Diet 86 (obtained from Messrs. Dixon, Ware, Herts.) and given water *ad libitum*. They were examined at weekly intervals, a note being made of the condition of the implantation site on each occasion. Animals which developed large tumours at the injection site or elsewhere, and animals which were sick for any reason, were killed and examined post-mortem. Tissue from the implantation site of every rat and tissues from other organs showing pathological change, including all lesions suspected of being neoplastic, were taken for microscopic examination.

RESULTS

The survival of rats and the incidence of sarcomas at the site of implantation of sponge in different groups are shown in Table 1. It is obvious, both from the incidence

Table 1. Incidence of sarcomas in response to implantation of pieces of polyvinyl sponge of different shapes and sizes

Group	Size and shape of implant (mm)	Volume of implant (mm^3)	Cumulative total of sarcomas* at implantation site/survivors — Time (Days) 0	100	200	300	400	500	600	700	800
CB stock rats											
1	20 × 20 × 5	2000	0/24	0/24	0/23	2/20	5/19	8/11	8/4	9/1	9/0
2	20 × 20 × 2	800	0/24	0/24	0/24	0/23	0/22	0/18	0/13	1/6	1/4
3	12·6 × 12·6 × 5	800	0/24	0/24	0/24	0/22	1/19	2/15	3/8	4/3	5/0
4	33 × 33 × 2	2000	0/24	0/24	0/23	0/22	0/20	0/17	1/8	1/3	1/1
5	8 × 8 × 5	320	0/24	0/23	0/20	0/19	0/18	0/13	0/5	1/1	1/0
Inbred Woodruff hooded rats											
6	20 × 20 × 5	2000	0/24	0/24	0/24	0/24	1/23	6/17	8/11	10/10	12/1

* Note that fibromas were also seen at the injection site in two rats with sarcomas (see text).

of sarcomas and from the time of their appearance in the different groups, that the risk of sarcoma induction is related much more closely to the thickness of the implant than to its volume. Of the two groups which were implanted with 2000 mm^3 pieces of sponge, Group 1 developed nine, and Group 4 only one sarcoma, despite better survival in the latter. If the survival difference is ignored, the difference is highly significant ($\chi^2 = 7{\cdot}4$ on 1 d.f.; $0{\cdot}01 > P > 0{\cdot}001$). Similarly, more tumours were seen in Group 3 than in Group 2, though both received the same dose of sponge (800 mm^3) and survival was better in Group 2. In this case the difference was not quite significant ($\chi^2 = 3{\cdot}05$ on 1 d.f.; $0{\cdot}1 > P > 0{\cdot}05$).

The incidence of sarcomas in the hooded rats in response to 20 × 20 × 5 mm implants was similar to that in the CB stock rats of Group 1. Survival was rather better in this group, however, so that the final incidence of tumours appeared slightly higher.

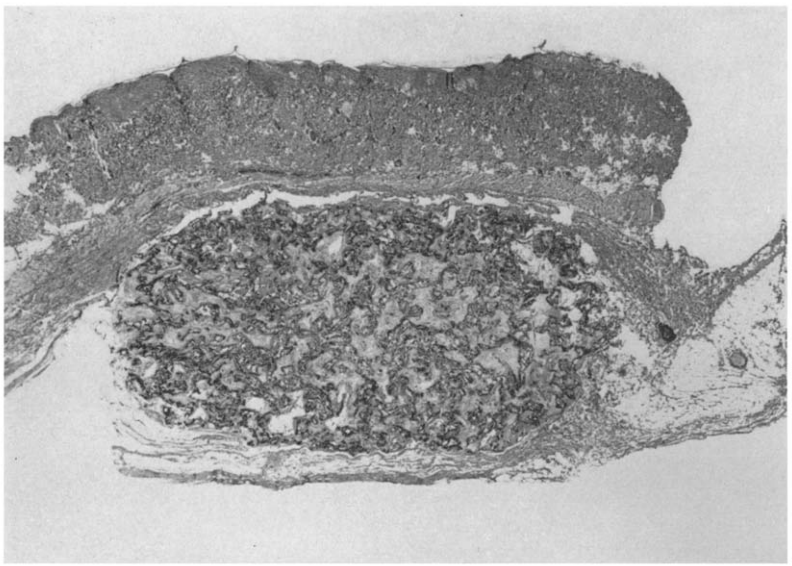

FIG. 1. Section through polyvinyl plastic sponge implant from animal of Group 5 killed 17 months after start of experiment. The sponge substance appears black and the interstices of the sponge contain fibrous or loose connective tissue. H and V.G. × 6·5.

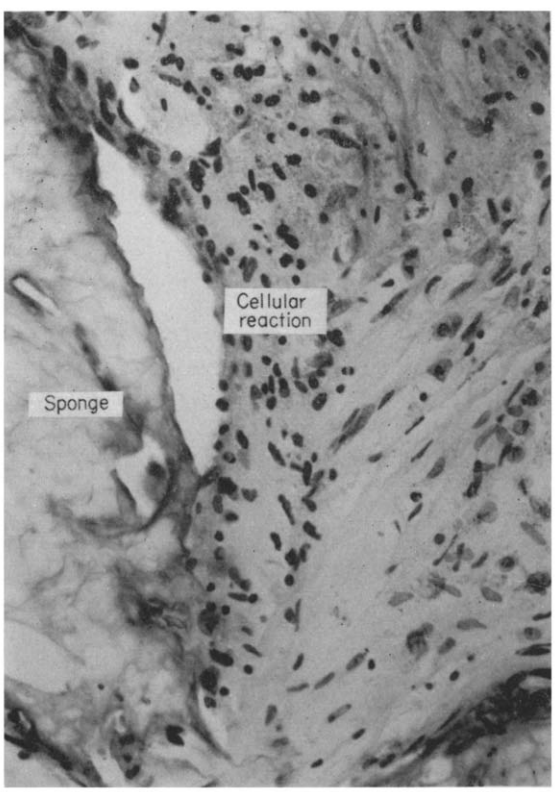

FIG. 2. Same as Fig. 1, showing cellular reaction to sponge. H and E × 310.

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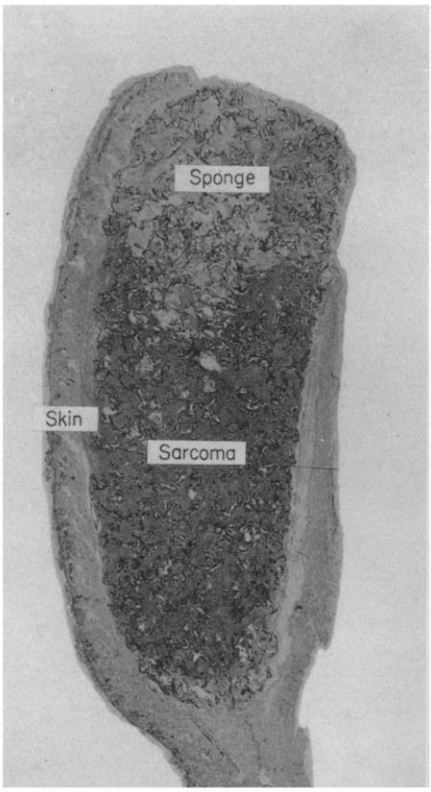

FIG. 3. Sponge from rat in Group 6, 23 months after implantation. Two thirds of the implant is invaded by a well circumscribed sarcoma. H and E × 4·6.

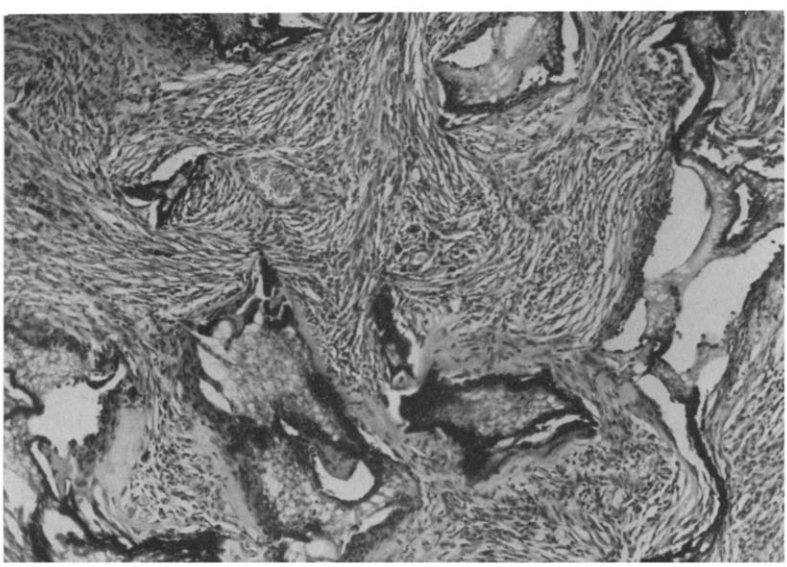

FIG. 4. Same as Fig. 3, showing spindle cell structure of carcoma. H and E × 105.

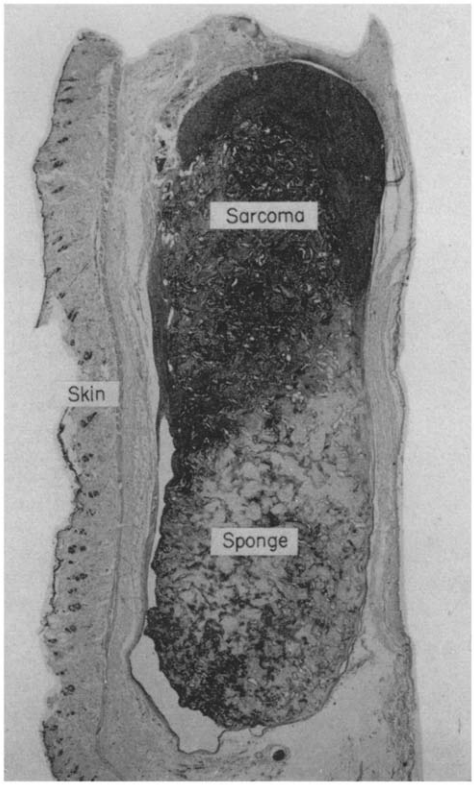

FIG. 5. Well circumscribed sarcoma within and partly surrounding sponge implant in a rat of Group 1 killed after 20 months. H and E × 4·6.

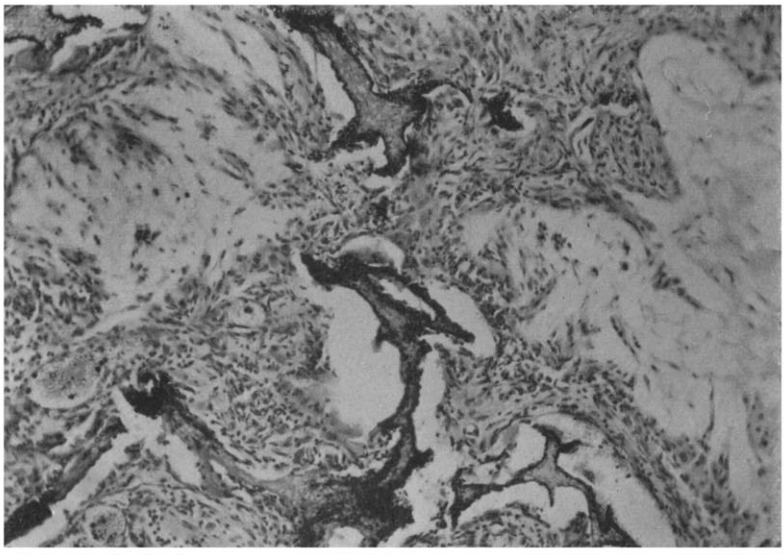

FIG. 6. Sponge from rat of Group 1 killed 23 months after implantation. Note the areas of myxomatous change which are often seen in association with early sarcomas. H and E × 105.

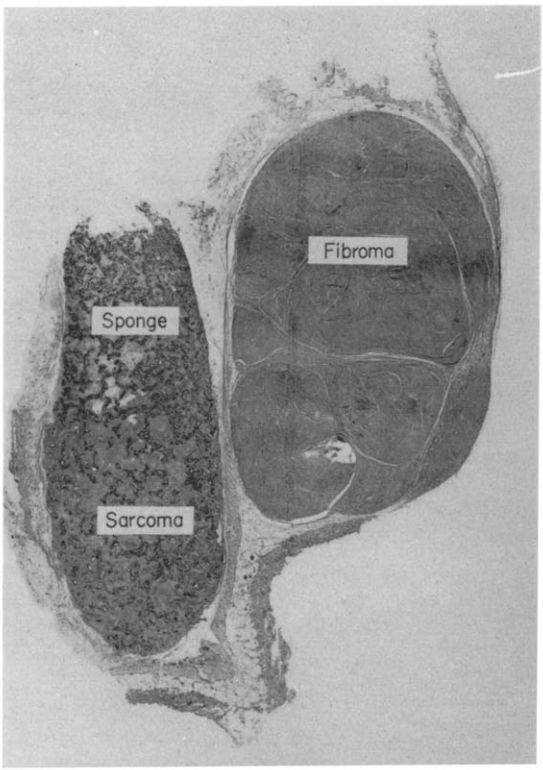

FIG. 7. Sarcoma arising in sponge and fibroma arising next to sponge in rat of Group 3 killed 23 months after implantation. H and E × 3.

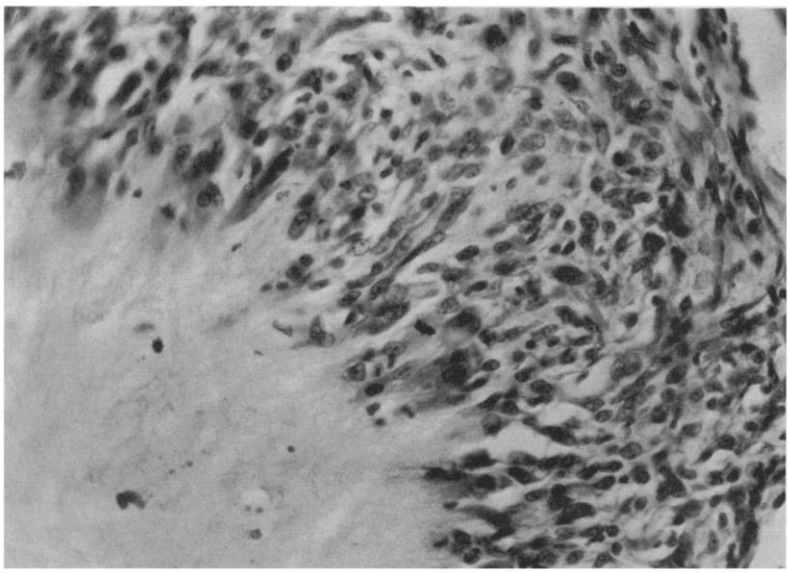

FIG. 8. Same as Fig. 7. Section through sarcoma with area of necrosis. H and E × 310.

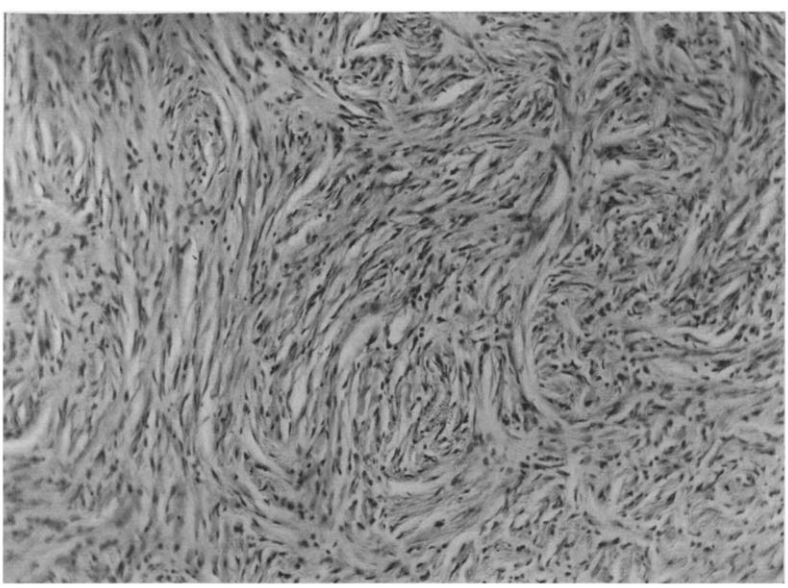

FIG. 9. Same as Fig. 7. Section through fibroma. H and E × 105.

Histological changes at site of implantation of sponge

Following implantation the interstices of the sponge are invaded by blood vessels, lymphocytes, plasma cells and macrophages. In the course of time fibroplasia ensues and fibrous tissue of varying density becomes prominent (Figs. 1 and 2). At any time after this stage has been reached, tumours, usually pleomorphic or spindle cell sarcomas (Figs. 3 and 4), may develop. Some appear to arise within the sponge and extend outwards (Figs. 3 and 4), whilst others seem to arise at the edge of the implant and invade the sponge secondarily. In many cases the exact origin of the tumour cannot be determined (Fig. 5). Sometimes, in association with early sarcomas, areas of myxomatous degeneration are seen (Fig. 6). In general, the sarcomas tend to be fairly well circumscribed though locally invasive. Their true malignancy, however, is illustrated by the fact that one of the tumours in a rat of Group 1 gave rise to multiple metastatic deposits in the lung.

Fibromas as well as sarcomas arose at the injection site in two rats. In a twenty-three month old rat of Group 6 both the fibroma and the sarcoma arose within the sponge, whereas in a rat of similar age of Group 3 the sarcoma arose within the sponge and the fibroma alongside it (Figs. 7–9).

Examination of the implantation site in rats bearing thin implants revealed that the sponge had in many cases been broken up in small pieces and to some extent removed from the site, presumably by phagocytosis. There was far less fibrous tissue reaction in these animals than in those bearing thicker implants.

Incidence of neoplasms at other sites

Tumours, other than those at the implantation site, were seen in Groups 2–6. These are shown in Table 2. Their distribution between groups does not indicate

TABLE 2. INCIDENCE OF NEOPLASMS OTHER THAN AT THE INJECTION SITE

Group	Volume of sponge (mm^3)	Thickness of sponge (mm)		Neoplasm	Date of death in days
1	2000	5		None	
2	800	2	(i)	Thymic lymphoma	529
			(ii)	Mesothelioma	669
			(iii)	Spindle cell sarcoma in neck	690
			(iv)	Thymic lymphoma	807
3	800	5	(i)	Myxosarcoma of s.c. tissues	606
			(ii)	Lymphosarcoma of lung*	627
			(iii)	Adenoma of renal cortex	669
			(iv)	Thymic lymphoma	760
4	2000	2	(i)	Islet cell adenoma of pancreas	736
			(ii)	Malignant lymphoma	809
5	320	5	(i)	Lymphosarcoma of lung*	507
			(ii)	Spindle cell sarcoma in neck	529
			(iii)	Lymphosarcoma of lung*	592
			(iv)	Thymic lymphoma	701
6	2000	5		Adenoma of lung	718

* These rats also had chronic murine pneumonia with bronchiectasis. In rats with advanced chronic murine pneumonia localized tumours, histologically indistinguishable from lymphosarcomas, are sometimes seen. It is not certain whether such lesions are true neoplasms.

any relation to volume or thickness of sponge and therefore does not suggest that the implantation of polyvinyl sponge was responsible for their occurrence.

DISCUSSION

It has long been suspected that rats and mice are more susceptible than other species to the induction of sarcomas by the injection or implantation of various materials. Because of the ease with which such tumours are induced, even by agents which seem to be without carcinogenic activity when administered by any other route, it is difficult to extrapolate the results of the present experiment to man. On the other hand, Dukes and Mitchley,[1] who also reviewed the relevant literature, described the histological appearances of sponges removed from humans after various periods of implantation, and it is clear from their report that, though the time scale is different, the early response of the tissues to implantation of sponge in man may be very similar to that in the rat.

Sponge implants have not been in use long enough in surgery to provide either evidence of their carcinogenicity in man or assurance of their safety. Clearly some carcinogenic risk may be entailed in their use and this risk may be high where large implants are used. In future, where the use of polyvinyl sponge seems justified despite the risk, it would be advisable for the implants to be kept as thin as possible.

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REFERENCE

1. C. E. Dukes and B. C. V. Mitchley, *Br. J. plast. Surg.* **15**, 225 (1962).