amounts is not, so that in these experiments methylcholanthrene apparently exerted its effects as a growth promoter other than as an estrogen.

Summary. Methylcholanthrene pellets implanted into the thymus gland of young guinea pigs induced hyperplasia of Hassall's bodies and of the thymic reticulum near the pellet, squamous epithelialization of the pellet space, small epithelial cysts, and degeneration of the small thymocytes. These new epithelia show intercellular bridges and keratohyaline formation, and since they arise from Hassall's bodies they show the epithelial nature of the latter.

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Influence of Sex on Resistance to Intraperitoneal Inoculation of Sarcoma in Mice.

LUDWIK GROSS. (Introduced by L. H. Schmidt.)

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Previous studies performed in this laboratory have shown clearly that adult male mice are more susceptible than females to intradermal inoculation of sarcoma S 37, as evidenced by the greater incidence of takes and the lower incidence of spontaneous regression of the cutaneous tumors produced in males.[1]

Experiments reported in this paper were carried out to determine whether this difference in resistance between males and females is demonstrable only following intradermal inoculation of sarcoma or whether a similar sex difference can be demonstrated following implantation of this tumor by another route such as the intraperitoneal route of inoculation.

Experimental. Groups of male and female mice were inoculated intraperitoneally with equal doses of cell suspensions of sarcoma S 37. Tumor-cell suspensions, varying in concentration from 1 to 20%, were prepared in the usual manner[1] and injected with a tuberculin syringe and a 27-gauge needle. Sexually mature male and virgin female mice of the albino E. S. strain[2] were used throughout this study. These animals were 2 to 3 months old and weighed 18 to 24 g.

Eighteen of the 209 males and 51 of the 224 females did not react to the inoculation. The remaining 191 males and 173 females de-

1 Gross, L., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 273.

2 Gross, L., *Cancer Research*, 1941, **1**, 880.

veloped tumors, which could be detected in the peritoneal cavity by palpation within 6 to 22 days after intraperitoneal inoculation. These tumors grew progressively and were uniformly fatal within 10 to 53 days following inoculation, the average survival time being 17.4 and 19.5 days for males and females respectively. At autopsy single or multiple sarcomatous tumors were found in the peritoneal cavity; in many cases hemorrhagic ascites were also present. In addition, many animals developed tumors in the abdominal wall at the point where the inoculating needle pierced the skin, muscles and peritoneum.

As shown in Table I, substantially more males than females developed fatal tumors following intraperitoneal inoculation of small doses of sarcoma. Only 12 of 101 males did not develop tumors as compared with 45 of 110 females. There was only one experiment in which more females developed tumors than males, and the number of animals in this experiment was very small.

This difference in resistance between males and females was discernible, however, only when the more dilute suspensions of tumor cells were inoculated. As shown in Table II, larger doses of sarcoma produced fatal tumors in practically all animals of both sexes—only 6 of 108 males and 6 of 114 females failing to react. The slight

TABLE I.
Intraperitoneal Inoculations of Small Doses of Sarcoma S 37.

Exp. No.	Tumor suspension		Sex	No. of mice inoculated	No. of mice died with tumors	% mortality
	% conc.	cc inj.				
1	1	.03	M	18	15	83
			F	21	11	52
2	1	.10	M	20	17	85
			F	21	7	33
3	1	.30	M	17	13	76
			F	19	10	53
4	5	.03	M	5	4	80
			F	5	5	100
5	5	.03	M	20	19	95
			F	21	12	57
6	10	.03	M	5	5	100
			F	5	3	60
7	15	.03	M	16	16	100
			F	18	17	94
Summary Exp. 1-7						
			M	101	89	88
			F	110	65	59

TABLE II.
Intraperitoneal Inoculations of Medium and Large Doses of Sarcoma S 37.

Exp. No.	Tumor suspension		Sex	No. of mice inoculated	No. of mice died with tumors	% mortality
	% conc.	cc inj.				
8	20	.03	M	10	10	100
			F	10	10	100
9	20	.03	M	10	8	80
			F	10	10	100
10	20	.03	M	6	6	100
			F	6	3	50
11	20	.05	M	10	10	100
			F	10	10	100
12	20	.06	M	15	15	100
			F	15	15	100
13	20	.10	M	5	5	100
			F	5	5	100
14	20	.15	M	17	14	82
			F	18	17	94
15	20	.20	M	15	15	100
			F	14	14	100
16	20	.20	M	20	19	95
			F	26	24	92
Summary Exp. 8-16						
			M	108	102	94
			F	114	108	95

differences in the reactions of males and females in experiments 9, 10, 14 and 16 are probably without significance.

In the 2 series of experiments just mentioned, tumors failed to develop in 18 males and 51 females—at least no tumors could be detected in these mice by careful palpation. All 18 of the males and 29 of the females were sacrificed 48 to 56 days after inoculation; no tumors were found at autopsy of these animals. The remaining 22 females were observed for 2½ months after inoculation, then were reinoculated intradermally with 0.03 cc of a 20% sarcoma cell suspension; as controls, 20 normal female mice were inoculated simultaneously with the same tumor dose. Nineteen of the 22 reinoculated females and 18 of the 20 control animals developed sarcomas. This is an additional indication that the previous, intraperitoneal inoculation was unsuccessful, since it is known that mice that have recovered spontaneously from a successful inoculation of tumor usually resist reinoculation with the same neoplasm; this is especially true of females.[2]

Discussion. According to experiments reported in this paper, the incidence of takes following *intraperitoneal* inoculation of small doses of sarcoma S 37 was substantially higher in male than in female mice; this difference in the resistance of males and females was abolished entirely by inoculation of larger doses of this tumor. These findings are essentially identical with our previous observations[1] on the incidence of takes following *intradermal* inoculation of the same sarcoma.

It is interesting to note that Bittner[3] and Strong and his coworkers[4] have observed a similar difference in the incidence of takes in male and female mice inoculated subcutaneously with transplantable carcinomas. In their experiments no attention was paid to the importance of careful dosage of the tumors. The results that we have obtained in both intradermal and intraperitoneal inoculations of sarcoma S 37 show that careful dosage of the tumor-cell suspension is most important for demonstrating at will the influence of sex on resistance to implantation of a neoplasm. Without careful dosage of the tumor, a difference in the incidence of takes in males and females may occur only accidentally. The trocar method of grafting tumor tissue, which has been used by most investigators in the study of transplantable neoplasms, makes it almost impossible to control the tumor dosage carefully. This may explain why no convincing evidence of a sex difference in the incidence of takes was obtained previously.

As shown in the present study, tumors produced by intraperitoneal inoculation of sarcoma S 37 were uniformly fatal. Spontaneous regression of such tumors was not observed either in males or in females. This result is in marked contrast to our previous findings concerning the spontaneous regression of tumors produced by *intradermal* inoculation of the same sarcoma.[1] It should be pointed out that the most remarkable difference between the reaction of males and females to intradermal inoculation of sarcoma was the low incidence of spontaneous recovery from tumors resulting in males as compared with that in females. This sex difference in the incidence of spontaneous regression of tumor seems to be more independent of dosage than the difference in the incidence of takes.[2]

The difference in resistance of males and females to tumor implantation does not seem to be limited to mice, for Greene[5] has

[3] Bittner, J. J., *Am. J. Cancer*, 1932, **16**, 322.

[4] Strong, L. C., Hill, R. T., Pfeiffer, C. A., and Gardner, W. U., *Genetics*, 1938, **23**, 585.

[5] Greene, H. S. N., *J. Exp. Med.*, 1940, **71**, 305.

observed that twice as many takes occurred in male as in female rabbits following transplantation of a spontaneous tumor into the anterior chamber of the eye; moreover, Greene found that all grafts which progressed to the extent of corneal invasion occurred in males.

Summary and Conclusion. Following intraperitoneal inoculation of small doses of sarcoma S 37, 89 of 101 males (88%) developed tumors, as compared with 65 of 110 females (59%). This difference in resistance between males and females was completely abolished by larger doses of sarcoma, which produced tumors in 102 of 108 males (94%) and in 108 of 114 females (95%).

Tumors produced by intraperitoneal inoculation of sarcoma were uniformly fatal and in no instance was spontaneous regression of such a tumor observed.

Comparison of these results with those obtained by intradermal inoculations of sarcoma S 37[1] suggests that careful dosage of the tumor-cell suspension and the route of inoculation are most important in demonstrating the influence of sex on resistance to transplantable neoplasms. Neither of these factors has been stressed sufficiently, heretofore, in studies on the evolution of implanted tumors in different sexes.

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Experimental Atherosclerosis and Soya Lecithin.*

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The well established lipotropic property of lecithin in the prevention of fatty livers and the partial protection apparently afforded by soy bean flour against cholesterol-induced atherosclerosis in rabbits,[2] suggested the investigation of the effect of soya lecithin on experimental atherosclerosis. Accordingly 23 young adult chinchilla rabbits were divided into 3 groups. All were fed 150 mg of cholesterol daily in oil added to a basic diet consisting of white flour, alfalfa, linseed meal, carrots and salt mixture.[1] Group A received nothing more. Rabbits of Groups B and C received 5 g and 1 g respectively in the diet daily of crude soya lecithin (approxi-

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