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ANGIOGRAPHY OF THREE MALIGNANT TUMORS TRANSPLANTED INTO YOUNG, MIDDLE-AGED, AND OLD MICE

by

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The purpose of this paper is to compare the growth rates and vascularity as seen by angiography in three transplanted malignant tumors in young, middle-aged, and old host mice.

Material and Methods. Three age groups of mice (young, middle-aged, and old) served as hosts for transplanted rhabdomyosarcoma, lymphosarcoma, and hepatoma. A total of 145 C3H (Jackson Memorial Laboratory) and strain 129 (Washington University School of Medicine) mice were used for this purpose.

Rhabdomyosarcoma. This tumor was originally obtained in 1950 from Dr Elizabeth U. Green's Laboratory in its seventieth transplant generation. The tumor was first induced by the intramuscular injection of 0.5 mg of 20-methycholanthrene suspended in filtered lard. The tumor appeared 71 days after the injection of carcinogen and was transplanted 24 days thereafter. The recipient strain was C3H but was later changed to (C3H × DBA) F1 hybrids. The C3H

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Table

Tumor type	Host mouse strain	Definition of age of host (months)			Number of hosts		
		Young	Middle-aged	Old	Young	Middle-aged	Old
Lymphosarcoma	C3H	3	9	16	21	17	18
Hepatoma	129L	3	12—15	21—25	12	16	9
Rhabdomyosarcoma	C3H	3	9	16	18	11	23

mice which were to receive tumor transplants were shaved in our laboratories and the area was disinfected with 70 % alcohol. The tumor to be implanted was excised, cut into small pieces, washed in isotonic saline containing 50 % streptomycin and 2.5 % penicillin, and transplanted subcutaneously to the recipient animal by trocar. After 6 to 7 days the transplanted tumor was easily palpated under the skin.

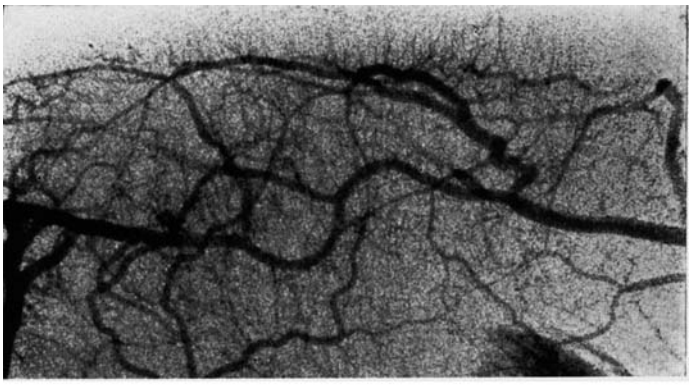
The mice in group I (young) were 3 months, those in group II (middle-aged) 9 months old, and those of group III (old) 16 months old. A 100 % growth of the tumor transplant was obtained in all three groups. Radiologic observations were made three weeks after transplantation.

Lymphosarcoma. This tumor was also carried in C3H mice. It grew extremely fast, especially in young mice. The tumor, however, was characterized by such diffuse growth in the subcutaneous tissue of the host that its accurate measurement was difficult. Transplantation was accomplished as described for rhabdomyosarcoma, except that antibiotics were not used. The tumor-bearing mice were in identical age groups as those bearing rhabdomyosarcoma.

Hepatoma 129L. This tumor arose spontaneously in an old male mouse of strain No 129 in May, 1957, and was transplanted to mice of the strain by the procedure described for lymphosarcoma. Since that time the continuance of this tumor has been maintained in Wernse Laboratory of Washington University School of Medicine.

The growth of hepatoma No 129L was extremely slow. Microscopically it greatly resembles normal liver cells, but the pattern of the liver is completely lost and numerous mitoses are observed. Since mice of strain No 129 live longer than C3H mice, those of the following age groups were used: I (young) were 3 months, II (middle-aged) were 12 to 15 months, and III (old) were 21 to 25 months old. The tumor take was 90 %.

Angiography was performed when the tumors were approximately 1 to 1.5 cm in size. Thorotrast was injected into the left ventricle of the heart via a



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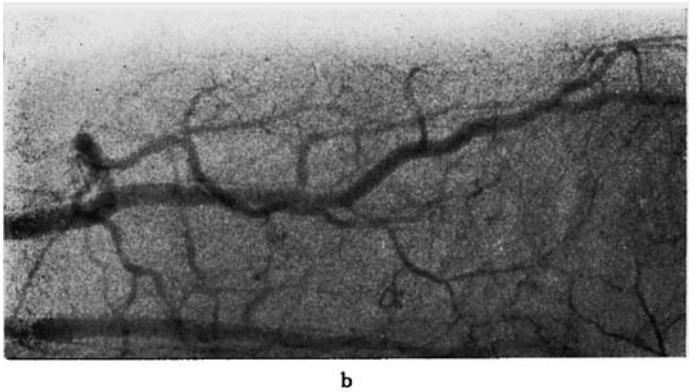

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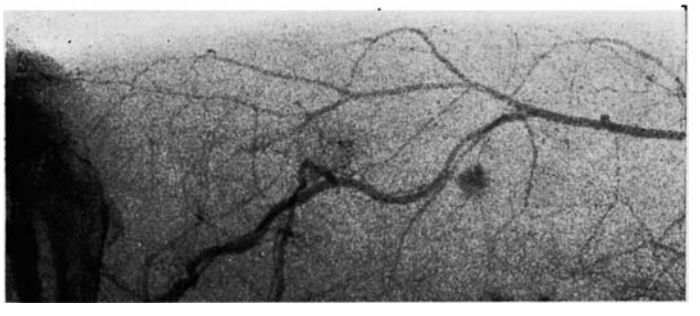

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Fig. 1. Lymphosarcoma. a) Young host. b) Middle-aged host. Some diminution of vascularity. c) Old host. Further decrease in number and size of vessels in tumor and its bed.

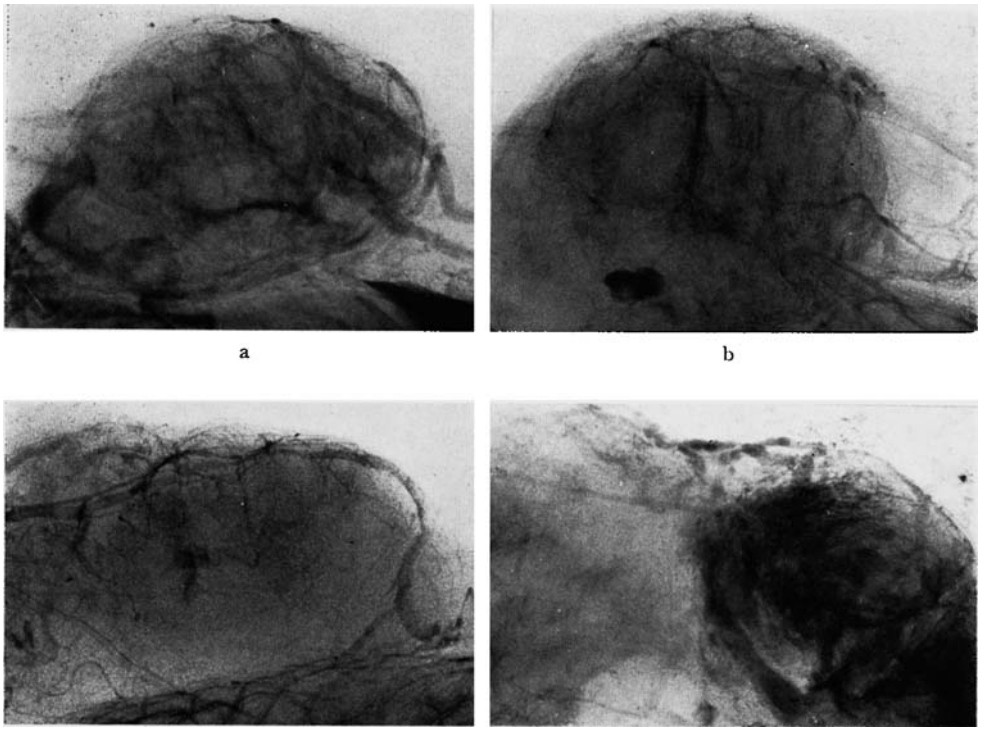

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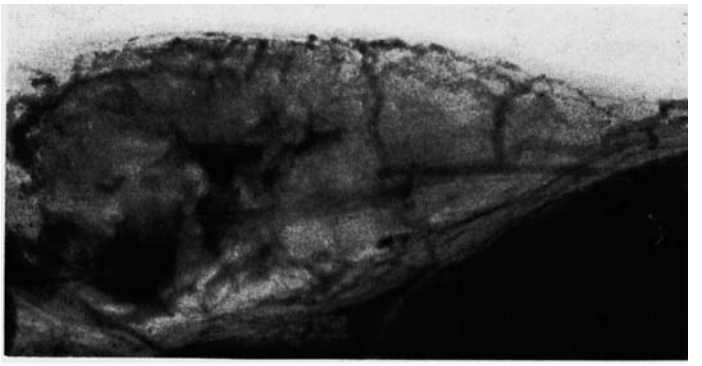
Fig. 2. Hepatomas. a) Young host. b) Middle-aged host. Decrease in number of vessels in tumor and its bed. c) Old host. Further decrease in vascularity. d) Middle-aged host. One lobule more vascular than the other.

catheter as previously reported (MARGULIS et coll. 1961). Serial radiographic exposures were made during the filling of the vascular system. The angiograms of the tumor and its bed were then enlarged ten times photographically.

The angiograms were studied for appearances, abundance, and distribution of the vessels in the tumor and its bed. The relative numbers of large and small vessels were compared, and individual vessels were studied for tapering, tortuosity, and abrupt endings. The collections and amount of contrast medium ('lakes') were recorded. The tumor type, strain, age and number of host mice are given in the Table on p. 18.

Results

Growth of lymphosarcoma was fastest and that of hepatoma slowest. The growth rate of lymphosarcoma was found to be higher in the younger than in the older host mice. Tumor growth of rhabdomyosarcoma varied greatly



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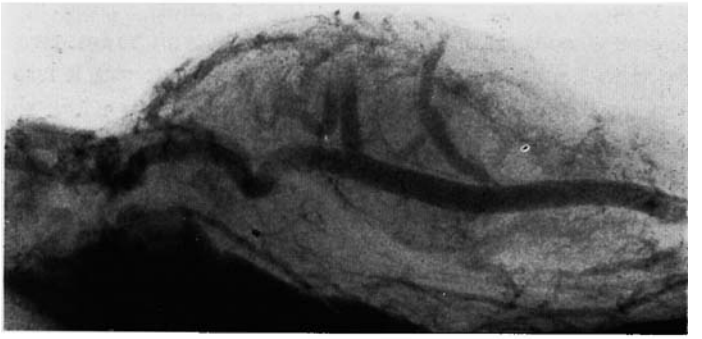

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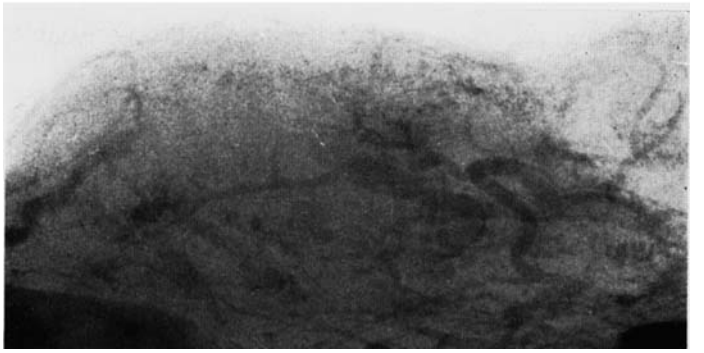

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Fig. 3. Rhabdomyosarcomas. a) Young host. A highly vascular tumor with multiple 'lakes' or collections of contrast material. b) Middle-aged host. Slight decrease in vascularity. c) Old host. Definite decrease in vascularity including 'lakes'.

but little difference in the average growth rate of the tumor was noted in the three age groups.

Hepatoma transplants did not grow as well in old mice but the rate of growth in age groups I (young) and II (middle-aged) was similar. No indication of growth of the tumor in group III can be given with certainty because some of the mice died of old age before the tumor was large enough for use, but the growth rate appeared slower in old mice.

The vascularity was found to have decreased in all three tumors and their beds in old host mice (Figs 1c, 2c, and 3c). These findings were most striking in lymphosarcoma, less marked in hepatoma, and were present to a lesser degree in rhabdomyosarcoma. The character of the changes was similar in all three tumors in old mice, but differed in degree and incidence. The most frequent finding was a decrease in the number and size of large and small arteries and veins, as well as of unidentifiable small vessels. Tortuosity of arteries and veins was increased in tumors in old host mice but this finding was largely confined to hepatoma. 'Laking' was present but much less frequent in rhabdomyosarcoma and hepatoma in old host mice than when the same two tumors grew in young mice. The tumor bed vessels were decreased in old mice and closely paralleled the abundance and size of the vessels in the tumors. Again the changes were most striking in lymphosarcoma.

Tumors of young mice had vascular appearances as previously described (MARGULIS et coll. 1961). Typical patterns in the three tumors in the young host age group are illustrated in Figs 1a, 2a, and 3a.

The vascular patterns of the three tumors in middle-aged mice were somewhat unpredictable (Figs 1b, 2b, and 3b). In some tumors, especially in lymphosarcoma, the vascular anatomy was similar to that encountered in old mice. Other tumors in regard to vascularity were indistinguishable from those seen in young hosts.

Decrease in abundance and size of vessels in the hepatomas transplanted into middle-aged hosts was less than that observed in the same tumor growing in old mice both in degree and incidence (Fig. 2, b and c). In a few hepatomas in middle-aged mice, the vascular appearance of some lobules were similar to the features encountered in young hosts, whereas vascularity in other lobules in the same tumor was only scant (Fig. 2d).

SUMMARY

Transplanted lymphosarcoma, hepatoma, and rhabdomyosarcoma were studied in young, middle-aged, and old host mice. The growth rates of lymphosarcoma were definitely decreased in the old mice and to a lesser degree in middle-aged mice. Hepatomas did not grow as well in old mice. In rhabdomyosarcoma the rate of tumor growth did not differ in the three age groups. The vascularity of the tumor decreased in the lymphosarcomas and hepatomas of old mice hosts, to a lesser degree in rhabdomyosarcomas.

ZUSAMMENFASSUNG

Transplantierte Lymphosarkome, Hepatome und Rhabdomyosarkome wurden auf junge, ältere und alte Mäuse eingepflanzt und studiert. Die Wachstumsschnelligkeit von Lymphosarkomen war deutlich geringer in alten Mäusen und wenigstens etwas geringer in mittelalten Mäusen; Hepatome wuchsen nicht gut in alten Mäusen. In Rhabdomyosarkomen wurde kein Unterschied nach Altersgruppen festgestellt. Es fand sich eine geringere Vaskularisation in den Lymphosarkomen und Hepatomen der alten Mäuse, aber weniger ausgesprochen in den Rhabdomyosarkomen.

RÉSUMÉ

Les auteurs ont étudie des lymphosarcomes, des hépatomes et des rhabdomyosarcomes transplantés sur des souris jeunes, adultes et âgées. La croissance des lymphosarcomes est nettement ralentie chez les souris agées, et, à un moindre degré, chez les souris adultes. Les hépatomes croissent moins bien chez les souris âgées. Pour les rhabdomyosarcomes, la vitesse d'accroissement est la même dans les trois groupes d'âge. La vascularité des tumeurs est diminuée chez les souris âgées dans les lymphosarcomes et les hépatomes, mais moins dans les rhabdomyosarcomes.

REFERENCES

MARGULIS A. R., CARLSSON E., and MCALISTER W. H.: Angiography of malignant tumors in mice. Acta radiol. 56 (1961), 179.