Development of Tumor in Transplanted Lungs of Newborn and Adult Mice[1] (34822)

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It has been previously reported that newborn mice are more susceptible than adult mice in tumorigenic response of lung to the administration of chemical carcinogens (1, 2). In the present communication, the age factor which possibly influences the neoplastic responses of the animals to chemical carcinogens has been analyzed from the point of view of "age of organ." For such purpose, the incidence of pulmonary tumor in newborn and adult lung transplants was compared in the same hosts.

Materials and Methods. Mice of the A/Jax strain were used in this study. This strain of mice shows high incidence of pulmonary tumor, with incidences of spontaneous tumor development of 6, 38, and 64% in mice of 6, 12, and 18 months of age, respectively (3).

Both male and female mice 30–45 days of age were used as the hosts. A whole lung or a half of a lung was used as a transplant of newborn lung and one of four to six fragments of adult mouse lung (45 days of age) were prepared as an adult transplant. Each host was given newborn and adult lung transplants into the subcutaneous region of the right and left axillae, respectively, under nembutal anesthesia. The sex of the host was matched with that of the donor animal. Subsequently, a single dose of 0.2 mg of 3-methylcholanthrene dissolved in olive oil was injected intraperitoneally into the animals. The host animals were autopsied 15 weeks after the transplantation. The termination of the present experiment was decided on the basis of our data (1, 2) of the incidence of pulmonary tumor in this strain of mice which received a single subcutaneous injection of 0.1 mg of methylcholanthrene at birth or 0.2 mg of methylcholanthrene at adult age. The incidences were 30, 46, 84, 100, and 100% in mice at 4, 6, 8, 12, and more than 13 weeks after a neonatal injection, respectively; they were 17, 28, 37, 57, and 100% in mice at 6, 8, 12, 15–20, and more than 30 weeks after an injection at 26–66 days of age. The tissue transplants derived from both newborn and adult mice retained forms of nodules in the transplanted regions in all cases (Fig. 1).

Serial sections, 6μ in thickness, were cut out from the whole transplants after fixation and embedded in paraffin. The sections were stained either with hematoxylin and eosin or with Kreyberg and Jareg's tetrachrome (4), followed by observation under a microscope.

Results. As shown in Table I, the incidence of tumor in the lung transplants was significantly higher in transplants derived from the newborn mice than in those obtained from adult mice ($\chi^2 = 5.8$). Micrographs of the pulmonary tumors that developed in transplanted lung of newborn and adult mice are shown in Figs. 2, 3, and 4, respectively. His-

TABLE I. Difference in Susceptibility to Tumorigenic Responses of Lung Transplants Derived from Newborn and from Adult A/Jax Mice to 3-Methylcholanthrene.

No. of mice	Number of mice with tumor in transplanted lung[a,b]							
	N +	A +	N +	A −	N −	A −	N −	A +
19	8		8		2		1	

[a] Tumor incidence in transplanted lungs derived from newborn mice = 16/19; tumor incidence in transplanted lungs derived from adult mice = 9/19; $\chi^2 = 5.8$.

[b] N = newborn; A = adult.

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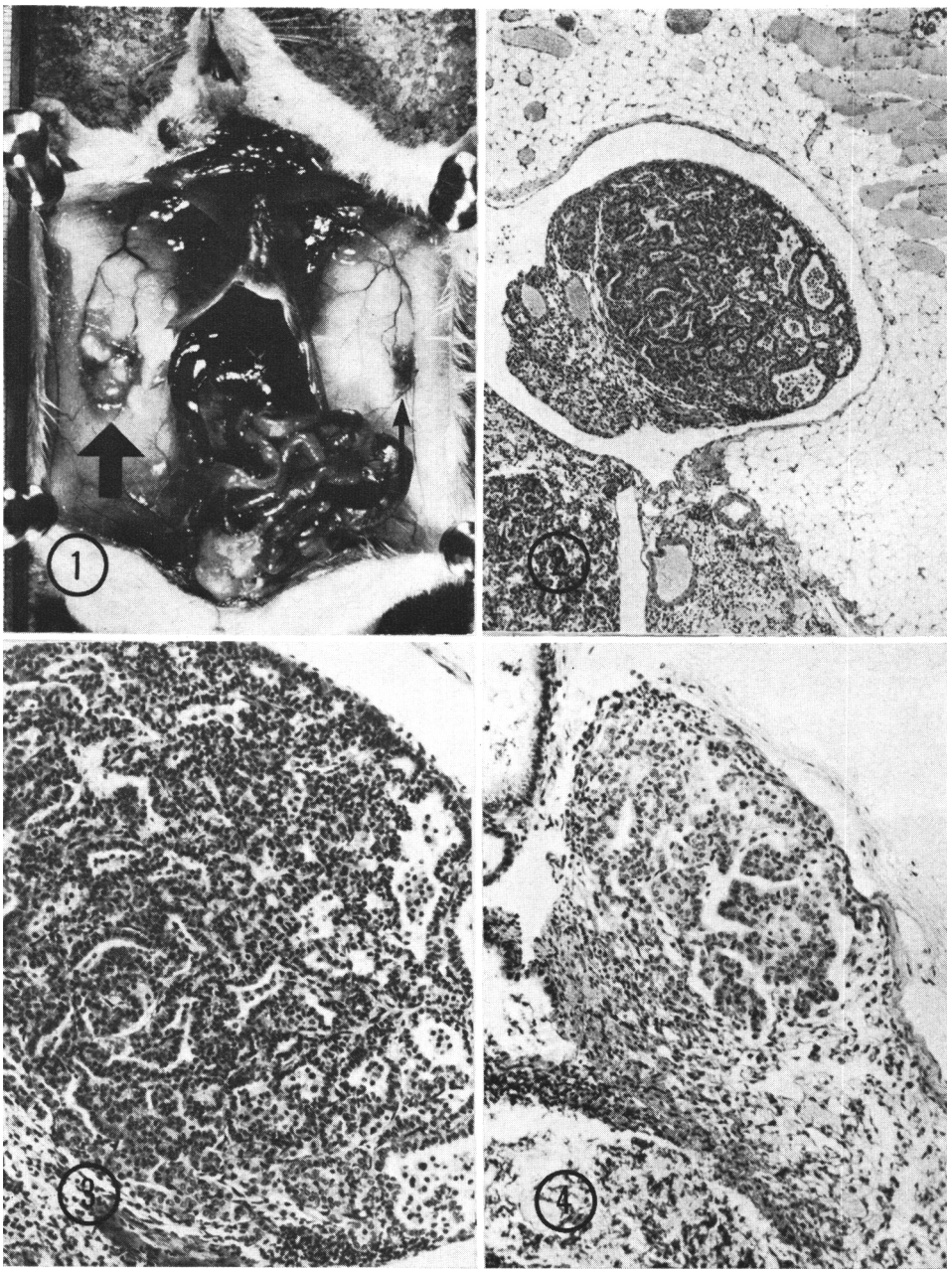

FIG. 1. Both lung transplants obtained from newborn (bold arrow) and adult (slender arrow) mice remained well in the subcutaneous regions. The tumors were found in the right transplant which was obtained from a newborn mouse.

FIG. 2. Low-power view of a tumor growing in a transplant derived from a newborn mouse. ×57.

FIG. 3. Higher magnification of the tumor in Fig. 2. The tumor grew in a papillary pattern which was identical with that of a primary pulmonary tumor in lung region. ×147.

FIG. 4. A small tumor observed in a transplant derived from a lung of an adult mouse. ×147.

tologically, they are identical to the primary lung tumors which developed spontaneously or were induced by the carcinogen.

Discussion and Summary. After terminating the present series of experiments, we found in the literature that Heston had employed the analogous methodological approach in order to confirm the difference in degree of genetic susceptibility to tumor formation in susceptible strain A and resistant strain C57L lung and had shown that the genetic factor of the susceptibility to the development of pulmonary tumor in mice resides in the lung *per se* (5).

In order to explain the reason of higher susceptibility in the newborn animals to chemical carcinogenesis, Toth itemized the following alternatives: (1) detoxification and metabolism rates of carcinogenic chemicals are different in newborn and adult animals; (2) the rate of development and size of organs in newborn is greater than in adult animals; (3) involvement of a viral factor; (4) the effect of hormonal status modulated by the age of the animals; and (5) the possible interference of immunological processes (6).

In the present study an attempt was made to clarify the difference in susceptibility to tumor formation between lung transplants of newborn and adult mice. The fact that the lung transplant from the newborns possesses higher susceptibility to the tumorigenic action of methylcholanthrene than those from the adults leads to the conclusion that the age factor which influences the tumorigenic responses in lung to the administration of methylcholanthrene is located in the lung of the mouse itself.

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