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Temperature Level and the Growth of Embryo and Tumor of Tumor-Bearing Eggs.

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The technique of growing tumor tissue in embryonated eggs has been routine in this laboratory for more than 4 years. The use of the yolk sac method of inoculation has made it comparatively simple to maintain rat and mouse tumors indefinitely by egg to egg inoculations.[1,2]

The size of the tumors grown in this manner were of the same order as those obtained by transplant in the host animal. This continued to be so after as much as 114 transplant-generations or about 4 years continuously in eggs. Apparently the egg environment satisfies all the requirements of malignant tissue for vigorous growth.

The inoculation of eggs through the yolk sac results in tumor implantation on the yolk sac inner wall.[3] In this situation the growth of the tumor presents a minimum of interference with the development of the chick embryo. Tumor tissue and chick tissue grow together sharing a common blood supply. It is not uncommon for the egg-grown tumor to weigh as much as 6 g at the 17th day of egg incubation, while the chick embyro normally weighing about 20 g at this stage is reduced to 10 or 12 g.

The egg environment is relatively stable but a certain amount of manipulation will be tolerated by the chick embryo. This is especially so with respect to temperature. Incubating eggs will withstand considerable variation in temperature and still survive to the 17-18 day period.

The present paper is concerned with a study of the comparative reactions of tumor and chick tissues grown together to temperatures above and below that required for normal incubation.

Experimental. Embryonated eggs on the 4th day of incubation were inoculated with dba mouse mammary carcinoma. The eggs of one series of inoculations were divided into 3 groups and incubated from the time of implantation until the termination of the experiment at 3 different temperatures. One group representing the control was kept at 99-100° F, a second group was incubated at 96-97°F, and the third group was maintained at a temperature of 103-104°F. At the 18th day of incubation, or 14 days after tumor inoculation, the embryos and tumors of the surviving eggs were harvested and weighed. A total of 1179 eggs was inoculated with tumor tissue for this research involving 17 separate experiments.

The results are given in Table I. Statistical validity of the figures given has been checked and found to be beyond question.

The chick embryo was less affected by the higher- and lower-than-normal incubating temperatures than was the egg-cultivated tumor. This was particularly striking for the temperature range, 103-104°F, at which the chick embryos averaged a reduction in weight of 12% while the tumors grown in these eggs were reduced in size 50% as compared with their respective weights at the control temperature.

Previous work has demonstrated that in eggs inoculated by the yolk sac method the size of the embryo is generally conditioned by the size of the tumor.[4] A large vigorous

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[2] Taylor, A., Thacker, J., and Pennington, D., *Science*, 1942, **96**, 342.

[3] Hungate, R. E., Taylor, A., and Thompson, R. C., *Cancer Research*, 1944, **4**, 289.

[4] Kynette, A., Taylor, A., and Thompson, R. C., *Univ. of Texas Publication No. 4507, Cancer Studies*, 1945, pp. 65-75.

TABLE I.
Effect of Temperatures Above and Below Normal Incubation on Embryo and Tumor Weights of Tumor-Bearing Eggs.

No. exp.	Incubation temperature (°F)	No. eggs inoculated	No. eggs surviving	Avg. chick size (g)	Exp. chicks, control = 100	Avg. tumor size (g)	Exp. tumor, control = 100
17 (control)	99-100	397	165	11.8 ± 1.8	100	1.0 ± .4	100
17	96-97	392	145	10.1 ± 1.2	85.6	.6 ± .2	60
17	103-104	390	55	10.4 ± 1.0	88.1	.5 ± .3	50

tumor frequently occurs in the egg together with an anemic undersized chick embryo. It appears that the relation of the chick embryo to the tumor implanted in its yolk sac is comparable to the relation of the host mouse to a tumor growing from a transplant.

It seems probable therefore that the reduction in size of the egg-grown tumors in response to temperature level above and below 99-100°F was a direct effect. Further, the data indicate that the egg-cultivated tumors are more sensitive to this factor than the supporting embryos.

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The Tuberculin Reaction. I. Passive Transfer of Tuberculin Sensitivity with Cells of Tuberculous Guinea Pigs.*†

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It has been established that the "tuberculin type" of sensitivity is distinct from the anaphylactic or Arthus type of sensitivity and from the atopic type of sensitivity dependent upon Prausnitz-Küstner antibody.[1-6] Although it is probable that the tuberculin type of sensitivity depends upon an antibody, the existence of such an antibody has not been established with certainty.

That tuberculin type sensitivity is dependent upon antibody is indicated by the similarities it shows to other sensitivities known to be dependent upon antibody, namely, similarities relating to specificity, incubation time, desensitization, anamnestic reaction, and the correlation between the ability of various animal species to form ordinary antibody and to develop tuberculin sensitivity. Supporting evidence is also provided by the observation that blockage of the reticulendothelial system which depresses the formation of ordinary antibody to an injected protein, likewise suppresses the development of tuberculin sensitivity.[7] In addition, it has been found that the use of adjuvants such as

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† The term sensitivity is used throughout this article in preference to the more commonly used term hypersensitivity.

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2 Rich, A. R., Lewis, M. R., *Bull. Johns Hopkins Hosp.*, 1932, **50**, 115.

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4 Aronson, J. D., *J. Immunol.*, 1933, **25**, 1.

5 Moen, J. K., and Swift, H. F., *J. Exp. Med.*, 1936, **64**, 339.

6 Heilman, D. H., Feldman, W. H., and Mann, F. C., *Am. Rev. Tub.*, 1944, **50**, 344.