blood. However, in the quantity here used (5 cc. of serum) a negative reaction was obtained.

It is evident from the reactions obtained that the anterior pituitary-like hormone enters the fetal circulation through the cord but does not return in same concentration. In corroboration, Wislocki and Snyder[1] have demonstrated that the hormone fails to pass from the fetal circulation to the mother. It seems likely that it is fixed or destroyed in the fetal tissues.

To determine whether or not the hormone is stored in the liver, 108 gm. of liver obtained from a fetus dying *in utero* was extracted by means of 60% acid alcohol and the extract injected into[2] immature rats. The equivalent of 54 gm. (½ the total quantity obtained) was negative on 2 occasions. Apparently the hormone is not stored in the liver.

Examination of fetal ovaries fails to show any evidence of follicle maturation or luteinization. The uterus also shows no variation from the quiescent state. The hormone although entering the fetal circulation evidently does not act upon these structures. Further investigation is necessary to determine its fate in the fetus.

7267 P

Specificity of Enhancing Materials from Mammalian Tumors.

ALBERT E. CASEY.

From the Laboratories of The Rockefeller Institute for Medical Research.

That growth promoting substances are present in transplanted tumors has been known for a long time. But that they can exercise a profound influence over the metastatic phase of malignancy, that their effects in sensitizing the host to a malignant growth can be more or less permanent, or that they have species and tissue limitations in their activity is only now being demonstrated.[1] Thus, a filterable material from the Brown-Pearce rabbit tumor has been found to enhance every observed phase of the growth of this tumor, both local and metastatic. A species limitation has been noted in

[1] Wislocki and Snyder, PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 196.

[2] Zondek, B., *Hormone d. Ovariums u. des. Hypophysenvorderlappens.* Julius Springer, 1931, 200.

[1] Casey, A. E., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 869; 1933, **30**, 674, 1025.

that the material from the rabbit tumor would not enhance the growth of mouse carcinoma 63 or mouse sarcoma 180. Rabbits treated with the material were still profoundly hypersusceptible to both local and metastatic phases of the Brown-Pearce tumor 7 months after the last injection.[2] The growth promoting material described by Haaland[3] and Leitch[4] in mouse carcinoma 63 has been found to enhance growths of the same tumor but has had no enhancing effect on the growth of the rabbit tumor or the growth of mouse sarcoma 180.

That enhancing materials are to be found in sarcomata seemed evident from the work of Flexner and Jobling[5] and of Chambers and Scott.[6] To test the specificity and biology of sarcoma enhancing materials, experiments were undertaken of which the first 3 are here reported. In each experiment tumor tissue from mouse sarcoma 180 was anaerobically refrigerated for 14-60 days at 24°F., minced and ground without sand, and emulsified with normal saline (dilution 1-10). In one experiment the emulsion was filtered through a Berkefeld "V" candle. Of this emulsion 0.1 cc. was injected into the left groin of 10 mice; 2 weeks later the 10 mice and 10 control mice not previously treated were inoculated in the same groin with fresh sarcoma 180. The incidence of primary tumors in 30 treated mice was 24 (80%) as compared with 17 (56.7%) among the 30 controls ($X^2 = 3.78$, $n = 1$, $P = 0.055$, probably significant); at 20 days the average cubic volume of the 24 tumors in the treated animals was 1.421 cc. as compared with 0.432 cc. for the 17 tumors among control animals (difference = 0.989 cc. $\pm$ 0.266, $t = 3.726$, $P = 0.01-$, a very significant result). In parallel experiments 30 additional mice were injected with the same sarcoma 180 enhancing material; 2 weeks later these mice and 28 additional control mice were inoculated with fresh mouse sarcoma 37. At 17 days 22 (75.8%) of the 29 treated mice had sarcomata as compared with 23 (82.1%) among the 28 control mice ($X^2 = 0.508$, $n = 1$, $P = 0.5$ not significant); the average of 22 tumors in treated animals was 0.716 cc. as compared with 0.9 cc. for 22 tumors among the con-

[2] Casey, A. E., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 666.

[3] Haaland, M., *Proc. Roy. Soc. of London*, 1910, **82**, 293; *Lancet*, 1910, **1**, 787.

[4] Leitch, A., *Lancet*, 1910, **1**, 991.

[5] Flexner, S., and Jobling, J. W., PROC. SOC. EXP. BIOL. AND MED., 1907, **4**, 156; **5**, 16. Jobling, J. W., *Monographs of The Rockefeller Institute for Medical Research*, 1910, **1**, 52.

[6] Chambers, H., and Scott, T. M., *J. Exp. Path.*, 1924, **5**, 1; 1926, **7**, 33; *J. Path. and Bact.*, 1932, **35**, 283.

trols (difference = 0.184 ± 0.236 cc., not significant). In the third experiment the sarcoma 180 enhancing material was tested for its activity on the growth of mouse carcinoma 63 in a different series of mice, and although one experiment is not conclusive, a slightly inhibiting instead of an enhancing effect was obtained. In mouse sarcoma 180 tissue there is, therefore, a material separable from the cells which has a profound enhancing effect on the incidence and growth of the same tumor but has no enhancing effect on the incidence and growth of mouse sarcoma 37 or of mouse sarcoma 63.

In another series of experiments, the effect of the mouse carcinoma 63 enhancing material has been tried on mouse carcinoma 48.* Of 50 mice in 5 experiments treated with 0.1 cc. of the carcinoma 63 material 2 weeks before the inoculation of carcinoma 48, the incidence of primary tumors was 5 (10%) as compared with 10 tumors (24%) among the 49 control mice not treated ($X^2 = 0.095$, $n = 1$, $P = 0.8$, not significant); the cubic volume of the 4 tumors at 28 days in treated animals averaged 0.512 cc. as compared with 0.773 cc. for the 10 tumors in control mice (difference = 0.216 cc., not significant). In no single experiment was there any evidence of enhancement. On the contrary, there was a faint suggestion of an inhibiting influence in each of the 5 experiments. However, the low percentage of takes among the controls indicates that additional experiments should be performed.

By biological experimentation 3 distinct homologous tumor enhancing materials have been differentiated the one from the other, namely, that from the rabbit tumor, that from mouse carcinoma 63, and that from sarcoma 180. Each enhances growths of its own tumor but does not enhance growths of the other 2 tumors. Furthermore, since the mouse carcinoma 63 material did not enhance mouse carcinoma 48, and the sarcoma 180 material did not enhance mouse sarcoma 37, one might expect to find at least 2 biologically distinct carcinoma enhancing materials and 2 biologically distinct sarcoma enhancing materials in the same animal species. The only other explanation would be that sarcoma 37 is really a carcinoma and carcinoma 48 a sarcoma. The work is still in progress.

* The author is indebted to Dr. Wm. H. Woglom of the Crocker Institute for this tumor.