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Transformation of Virus of Rabbit Fibroma (Shope) into that of Infectious Myxomatosis (Sanarelli).

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Berry,[1] Hoffstadt,[2] and Hurst[3] have reported the transformation of fibroma virus into myxoma virus employing crude tissue suspensions of myxoma virus. Meck[4] and Hyde[5] were unable to confirm these observations. Recently Gardner and Hyde[6] have accomplished the transformation with 3 of 7 elementary body suspensions of myxoma virus. Hurst[3] has obtained positive results in 5 of 7 rabbits and Hoffstadt[2] in 7 of 20. The purpose of the experiments here reported was to amplify these observations and to study factors which might account for the inconsistent results.

A 10% suspension of a dermal tumor of virulent myxoma virus was heated for 35 min at 60° C in a water-bath, then kept in sealed ampoules at 4°C until used. This tissue suspension of heat-inactivated myxoma virus was submitted to the following procedures:

1. Serial testicular passage.
2. Mixture with (a) active fibroma virus, (b) attenuated fibroma virus, (c) agents producing reduction, inflammation, increase in virulence; and subsequent testicular injection or serial passage of these mixtures.

Serial testicular passage was performed by removing the inoculated testicle 7 days after injection. This testicular tissue was triturated; portions of a 10% suspension were mixed with heat-inactivated myxoma virus and injected into the testicle of another rabbit.

Two sets of experiments were performed at separate times with freshly prepared heat-inactivated myxoma virus. New Zealand rabbits weighing approximately 4½ lb were used throughout the experiments, and they were kept in isolated cages to prevent possible cross-infection. Temperature readings and observations were made daily.

Experiment I.

Group 1. 1 cc of heat-inactivated myxoma virus passed serially through 3 rabbits.

Group 2. 1 cc of heat-inactivated myxoma virus plus 0.5 cc of active fibroma virus passed serially through 3 rabbits.

Group 3. 1 cc of heat-inactivated myxoma virus plus 0.5 cc of active fibroma virus passed serially through 2 rabbits.

Group 4. Control group. Dermal and testicular tumors of active myxoma virus and active fibroma virus injected into normal rabbits.

Experiment II.

Group 1. 1 cc of heat-inactivated myxoma virus passed serially through 2 rabbits.

Group 2. 1 cc of heat-inactivated myxoma virus plus 0.5 cc of attenuated fibroma virus (long storage in glycerol, causing minimal lesions) injected into 4 rabbits.

Group 3. 1 cc of heat-inactivated myxoma virus plus 0.5 cc of active fibroma virus passed serially through 2 sets of 4 rabbits each.

Group 4. 1 cc of heat-inactivated myxoma virus plus 0.07 cc of active fibroma virus injected into 4 rabbits.

Group 5. 1 cc of heat-inactivated myxoma virus plus the following materials: (Each mixture was injected into 1 rabbit, except 2(a) which was tested in 5 rabbits.)

1. Reducing agents.
   a. 1 cc of 5% $CaCl_2$.
   b. 0.02 cc of 1:50 cysteine hydrochloride.
   c. 0.1 cc of 2% sodium thioglycolate.
2. Inflammatory agents.
   a. 0.5-1 cc of beef extract and aleuronat in olive oil.

[1] Berry, G. P., and Dedrick, H. M., *J. Bact.*, 1936, **31**, 50.

[2] Hoffstadt, R. E., and Pilcher, K. S., *J. Inf. Dis.*, 1941, **68**, 67.

[3] Hurst, E. W., *Brit. J. Exp. Path.*, 1937, **18**, 23.

[4] Meck, J. S., and Acree, E. G., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 387.

[5] Hyde, R. R., *Am. J. Hyg.*, 1936, **24**, 217.

[6] Gardner, R. E., and Hyde, R. R., *J. Inf. Dis.*, 1942, **71**, 47.

b. 1 cc of 24-hr broth culture of *E. coli.*
c. 1 cc of 10% suspension of vaccinia virus.

3. Virulence-enhancing agent.
a. 2 cc of 5% gastric mucin.

Group 6. Control group. Dermal and testicular tumors of active myxoma virus and active fibroma virus injected into normal rabbits.

Results. The Berry transformation was successful only in Group 3 of Experiment I. Rabbit 1 exhibited generalized myxomatosis on the 12th day after injection and subsequently recovered. Testicular tissue removed from this rabbit on the 7th day following injection produced typical fatal myxomatosis in two normal rabbits. The possibility of accidental infection of this transformation rabbit was eliminated because there were no myxomatous rabbits in the laboratory at the time.

Typical fibromatosis and myxomatosis were produced in the control group.

Attempts to facilitate the transformation by the use of attenuated fibroma virus and small doses of active fibroma virus were not successful.

Heat-inactivated myxoma virus was not reactivated by inflammatory, reducing, and virulence-enhancing agents, or by serial passage.

Discussion. The occurrence of the Berry transformation in only one of 21 rabbits emphasizes the observations of other workers that this transformation is not accomplished easily.[1,2,3,5,6] Our inability to reactivate heat-inactivated myxoma virus with diverse agents amplifies the evidence of Berry[7,8] and Gardner and Hyde.[6] Additional data are required to prove whether fibroma virus reactivates heat-inactivated myxoma virus or is actually transformed into active myxoma virus.

[7] Personal communication.

[8] Berry, G. P., and Dedrick, H. M., *J. Bact.*, 1936, **32**, 356.

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Initiation of Secretory Changes in Transplanted Mammary Adenocarcinoma of the Rat by Pituitary Lactogenic Hormone.*

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Secretory phenomena in a transplanted mammary adenocarcinoma (R2426), maintained in inbred August rats, have been described following treatment of hosts of either sex with 0.166 mg estradiol benzoate or 0.2 mg estradiol dipropionate twice weekly.[1] Subsequent experiments have demonstrated that daily injections of considerably smaller quantities of the hormones are equally effective in initiating these changes, which varied in degree from isolated foci of secretory vacuoles in the neoplastic cells, evident only on microscopic examination, to extensive transformation of tumors into lactating cystic masses containing thick milk-like fluid. Neoplasms of the latter type bore little resemblance to the original adenocarcinoma. Tumors were not influenced by the normal hormonal variation incident upon age or sex,[2] nor did castration, pregnancy and lactation, or testosterone propionate affect either their growth or their histologic characteristics.[1]

Experimental. It appeared of interest to ascertain the influence of the lactogenic

* Anterior pituitary lactogenic hormone was generously furnished by the Research Department of Parke, Davis & Co., Detroit, Mich.; progesterone and estradiol dipropionate by Ciba Pharmaceutical Products, Inc., Summit, N.J.

[1] Eisen, M. J., *Cancer Research*, 1941, **1**, 457.

[2] Eisen, M. J., *Am. J. Cancer*, 1940, **39**, 36.