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Inhibition of Brown-Pearce Rabbit Tumor with Filtered Homologous Tumor Material.

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In the course of some experiments with the Brown-Pearce rabbit tumor[1, 2, 3] an unusual inhibitory effect was noted following a single injection of 0.3 cc. of a Berkefeld "V" filtrate of fresh tumor given 2 weeks before the tumor inoculation. The experiment had not previously been tried and has not yet been repeated. It would not be reported here except that it is the only case of complete failure of the Brown-Pearce rabbit tumor to grow following intratesticular inoculation in some 7 years of experience involving approximately 100 different transplantations of the tumor, and approximately 1000 rabbits. This experience includes studies on some 20 pure breeds, and on various types of hybrids, particularly with the type of brown-gray hybrids used in the experiment; and the probability of a rabbit being free of tumor at the end of a 2 months' observation period was calculated to be 0.2306. The occurrence of all 6 animals in an experiment being negative by accident is, therefore, very unlikely ($P = 0.01$—).

Furthermore the 6 animals of this unusual group were identical as to source, age, weight, coat color, vigor, size of testicles, and body build with 36 other rabbits not receiving the filtrate and composing 6 additional groups inoculated on the same day in staggered order[3] in the same testicle with the same dosage of the same fresh tumor. One of the 6 additional groups was a control group and was not otherwise treated. Analyzed per animal inoculated, the incidence of primary tumors in this group was 50% and the tumors averaged 5.8 cc.; the incidence of metastatic tumors was 83.3%; the metastatic tumor averaged 53.0 cc. in volume per animal and was distributed over 6.3 metastatic foci; the mortality was 61.1% over a period of 59 days. The 5 additional groups were treated with various other homologous materials before tumor inoculation and had an incidence of primary tumors of 40% which averaged 3.8 cc.; the inci-

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1 Casey, A. E., *Am. J. Cancer*, 1934, **21**, 760.

2 Casey, A. E., *Am. J. Cancer*, 1934, **16**, 776.

3 Casey, A. E., *Am. J. Cancer*, 1936, **26**.

dence of metastatic tumors varied from 80 to 100% per group, and averaged 88.0%; the volume of metastatic tumor per group varied from 40 to 162 cc. per animal and averaged 94 cc.; the number of metastatic foci varied from 10.2 to 24.2 per group and averaged 13.9 foci; the mortality varied from 60 to 100% and averaged 71.4%; the longevity varied from 48 to 61 days and averaged 54.7 days. In contrast with this only one of the 6 animals receiving the filtrate of fresh tumor 2 weeks before the tumor inoculation developed a primary tumor and this was a small, entirely necrotic nodule of 3 cc. at the end of the experiment, an average per animal inoculated of 0.5 cc.; the incidence, volume and number of metastatic foci were 0 for the group; the mortality 0, and the longevity 61 days (termination of the experiment). This result was statistically at variance with the results in the other groups inoculated. This inhibition could not be explained on the basis of the materials and methods. None of the animals were of resistant strains such as, the Havana, Polish, and Himalayan breeds, and so far as could be determined were identical with the animals of the other groups.

No other explanation is at present tenable other than that the filtrate of the fresh Brown-Pearce tumor contained a material exerting an inhibitory effect on tumor transplantation. This cell-free filtrate suggests the inhibitory material found in chicken tumors and normal tissues of various animals by Murphy, Helmer, Claude, Sturm,[4] and others. The method of testing differs, however, in that the present filtrate was injected in a different site 2 weeks before the tumor inoculation, instead of being mixed with the tumor inoculum. The source differs in that it was obtained from and exerted its effect upon the same mammalian tumor. Attempts to confirm this observation will be made and the success or failure reported.

[4] Murphy, J. B., Helmer, O. M., Claude, A., and Sturm, E., *Science*, 1931, **73**, 268.