maintained on a low-casein diet. The growth ceased. It was resumed upon incorporation, into the phenanthrene diet, of l-cystine, dl-methionine but not taurine. 2. Assumption is made that phenanthrene is detoxicated in the rat to yield a mercapturic acid, the formation of which is responsible, at least in part, for the cessation of growth of rats ingesting phenanthrene.

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Identity of "Inhibitor" and Antibody in Extracts of Virus-Induced Rabbit Papillomas.

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Saline extracts of the virus-induced papillomas of domestic rabbits often contain something that inhibits or neutralizes the virus *in vitro*, as Shope first noted.[1] Serological studies have shown that when mixed with it the blood of rabbits carrying these papillomas also has in most instances the power to neutralize the virus *in vitro*.[2] Experiments were undertaken to learn whether the "inhibitor" procured from the papillomas may not be specific antiviral antibody of the sort present in the blood.

To test for "inhibitor", 10% extracts of freshly procured papillomas were prepared by grinding in sand, suspending in saline, and centrifuging at about 4400 rpm for 20 minutes in an angle-head centrifuge. The clear supernatant fluids were then mixed in equal parts with a Berkefeld filtrate of the virus-induced growths of cottontail rabbits, containing virus of known titer, incubated 2 hours at 37°C, and rubbed into scarified areas on the skin of normal domestic rabbits according to a titration technic already described.[2]

The papillomas of 13 domestic rabbits with high serum-antibody titers, as determined by virus-neutralization and complement-fixation tests,[2, 3] all yielded large amounts of the "inhibitor", extracts of the growths neutralizing completely or almost completely an amount of virus equal to 500 minimal infective doses. Similar growths of 6 domestic rabbits which had but little circulating antibody yielded

1 Shope, R. E., *J. Exp. Med.*, 1933, **58**, 607.

2 Kidd, J. G., Beard, J. W., and Rous, P., *J. Exp. Med.*, 1936, **64**, 63, 79.

3 Kidd, J. G., *J. Exp. Med.*, 1938, **68**, 703, 725, 737.

little or none of the "inhibitor", the extracts of these, prepared in the same way, having practically no capacity to neutralize virus.

To study further the relation between the "inhibitor" and antibody, pieces of the papillomas of 4 domestic rabbits, all produced by the same inoculum, were repeatedly removed and tested for yield of "inhibitor", the amount of antibody in the serum of the rabbits being determined concurrently. On the 21st day after inoculation with the virus, that is to say, only 7 to 10 days after the growths had appeared and before antibody could be detected in the blood in noteworthy amount, the papillomas yielded little or no "inhibitor". Later tests (37th and 111th days) showed that, as the serum-antibody titer of 3 of the rabbits rose, the amount of inhibitory substance that could be procured from the growths increased in direct proportion to the amount of antibody present in the serum. The fourth animal failed to develop any noteworthy amount of circulating antibody and the papillomas yielded none of the "inhibitor" in any test. Further experiments showed that when the production of humoral antibody was stimulated by intraperitoneal injections of a papilloma-virus suspension the amount of inhibitory substance procurable from a given papilloma underwent a corresponding increase.

None of the inhibitory substance could be detected in the sera or in saline extracts of the skin, muscle, and liver of 4 normal rabbits; nor did extracts of the Brown-Pearce tumor, which had grown in 2 rabbits uninfected with the papilloma-virus, exert any effect upon the latter. In contrast to these findings the "inhibitor" was present in extracts of the skin, muscle, and liver of 6 rabbits carrying papillomas and having considerable amount of antibody in their serum. The neutralizing effect of extracts of papillomas was regularly greater than that of extracts of other tissues from the same rabbit, but much less than that of a 10% dilution of its serum.

The "inhibitor", like the antiviral antibody,[2] exerts no discernible influence on the course of the papillomas, as repeated observations have demonstrated, these enlarging progressively or dwindling and vanishing, irrespective of their content of "inhibitor". Nor is antibody or "inhibitor" primarily involved in the "masking" of the virus in the papillomas of domestic rabbits, for these have failed to yield active virus on extraction even when little or no antibody was present in the blood of the hosts bearing them[4] and when no "inhibitor" could be detected in them.

All of the findings indicate that the "inhibitor" present in extracts of the virus-induced rabbit papillomas is actually specific antiviral

[4] Kidd, J. G., *J. Exp. Med.*, 1939, **70**, in press.

antibody. They raise the question whether the "inhibitor" found in extracts of chicken sarcomas[5] may not be of similar nature.

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Decreased Tolerance of Mice to Intraperitoneal Glucose Injections in Certain Neurotropic Virus Infections.*

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Certain neurotropic virus infections of mice cause a definite decrease in the tolerance of these animals to intraperitoneally injected glucose.

Glucose was dissolved in distilled water and injected intraabdominally into white Swiss mice in constant volumes of 0.05 cc per gram of body weight. The concentrations of glucose employed varied from 45 to 10%. Viruses were inoculated intracerebrally and test injections of glucose were generally given during the early stage of disease symptoms, normal controls being included whenever virus-infected mice received dextrose. The viruses utilized were rabies fixed virus, a neurotropic strain of herpes, St. Louis encephalitis and equine encephalomyelitis (Western strain). The work included in Table I covers many small experiments, all of which pointed in the same direction.

Table I indicates that 25 and 20% glucose killed almost all virus-infected mice, whereas most corresponding controls survived. The injection of glucose, in the case of those mice that survived, had no effect on the subsequent course of the above virus diseases; the surviving virus-infected mice developed symptoms of increasing severity and eventually died.

Intraperitoneal injections of glucose often cause immediate symptoms of peritoneal irritation which quickly subside, after which the mice appear normal for 15 minutes or more. They then act irritable,

5 Sittenfeld, M. J., Johnson, B. A., and Jobling, J. W., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 517; Murphy, J. B., and Sturm, E., *Science*, 1931, **73**, 266; Claude, A., *Am. J. Cancer*, 1939, **37**, 59.

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