In this study nicotinic acid or amide were not equivalent to the filtrate or the dermatitis factors in the nutrition of rats. Nicotinic acid or amide had no supplementary effect when combined with concentrates from rice polishings and with yeast adenylic or nucleic acid.

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Effect of the Papilloma Virus (Shope) Upon the Tar Warts of Rabbits.

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When the papilloma virus is injected into the blood stream of rabbits previously tarred on the ears for 1½ to 3 months, growths rapidly arise on the tarred skin, often in great numbers. Some are squamous cell carcinomas,[1] usually multiple, and frequently metastasing.* We have studied the phenomenon in more than 70 rabbits, with 90 tarred controls. In none of the latter has a cancer developed.

Many of the growths that follow upon injection of the virus appear where no localized proliferation was previously visible, but others derive from pre-existing tar warts, which start growing rapidly, alter in aspect, and not infrequently manifest malignancy. After tarring is stopped, most ordinary tar warts disappear and the others become indolent, whereas the virus-stimulated warts keep on enlarging. Some are now carcinomatous but may undergo conversion into characteristic virus papillomas, as a scrutiny of several hundred specimens has shown; and others have become hybrids, neither ordinary tar tumors nor ordinary virus tumors but peculiar papillomas of malignant appearance, which change to squamous cell carcinomas almost at once. Not a few of the warts, however, though greatly stimulated by the virus (as proven by weekly records of their size), retain the morphology of the tar tumors.

To learn more, opportunity was provided for the virus to infect tar warts *in vitro*. The warty tissue was punched from the ears, a

[1] Rous, Peyton, and Kidd, J. G., *Science*, 1936, **83**, 468.

* Using benzpyrene instead of tar, Lacassagne and Nyka have confirmed our findings (*Bull. de l'Assoc. Française pour l'Etude du Cancer*, 1937, **26**, 1).

slice taken for section, and equal portions of the hashed remainder were steeped for some minutes in Tyrode, and in a Berkefeld filtrate of Tyrode containing potent virus, respectively; after which they were implanted at corresponding situations in the leg muscles and subcutaneous tissue of the hosts. Four or 5 wart materials from each rabbit were so treated, as was also some of the tarred skin devoid of warting. Tarring was kept up during a few later days because of its presumptive general influence to favor proliferation. The warts utilized proved to be the familiar tar papillomas and carcinoids,[2] so called because, though having the histology of carcinomas, and often ulcerating and growing through the ear, they ultimately disappear or revert to the benign, papillomatous form, even though tarring is continued.

One implanted animal died 20 days later and 9 were killed after 38 to 64 days. None of the 44 wart materials steeped in Tyrode had given rise to a growth, nor had the skin specimens done so. Tiny cysts lined with ordinary, stratified squamous epithelium resulted from 5 of the former and from 4 of the latter, the others undergoing resorption. Ferrero[3] has reported similar findings.

Very different was the outcome with the tissues steeped in virus. Then the bits of skin regularly gave rise to nodules of papillomatous tissue such as form on direct implantation of the Shope papilloma.[4] Similar nodules resulted from the implantation of 15 of the 24 tar papillomas, 4 yielded nothing, and 3 gave rise to small cysts like those just described. From one of the remaining 2 a malignant papilloma arose, markedly different from the original wart, and from the other a multicentric growth retaining the distinctive morphology of the latter. Nodules of Shope papillomatosis resulted from 8 of the 20 virus-steeped carcinoids, while 9 yielded nothing. In the remaining 3 instances, growths of carcinomatous aspect developed. The morphological characteristics of the original carcinoid had been retained in 2 of these cases, and the growths, though invasive, were small. The third was large, anaplastic and notably aggressive, to all appearances a malignant cancer, with but slight resemblance to the original carcinoid and none to those Shope papillomas that invade the muscle in which they are implanted.[4]

The warts from which the implantation growths of cancerous aspect derived had been large at biopsy in 4 of the 5 cases, and much of their tissue had been left *in situ*. After tarring was stopped one

[2] Borst, M., *Z. f. Krebsforsch.*, 1924, **21**, 344.

[3] Ferrero, V., *Arch. per le Sc. Med.*, 1926, **48**, 78.

[4] Rous, Peyton, and Beard, J. W., *J. Exp. Med.*, 1934, **60**, 701.

of them continued to enlarge slowly, but became a benign papilloma histologically, while the other 3 disappeared. The biggest to disappear was 2.3 cm. across and had extended through the ear when about one-tenth of it was taken for steeping. The bits steeped in Tyrode yielded no growth, whereas those exposed to virus gave rise to the large, malignant tumor just mentioned.

It is common knowledge that extraneous viruses[5] can flourish in tumors. Some induce no evident change, while others cause necrosis or the formation of inclusion bodies. The papilloma virus causes no inclusions, but it stimulates tar tumors to active growth, brings about morphological alterations in many of them, frequently acts as the determining factor in their survival, and makes some take on forthwith the character of carcinomas.

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Nutritional Myopathy of the Gizzard in Turkeys.

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This communication illustrates the fact that different species of animals may react in quite diverse fashion to the same abnormal diet. When growing chicks are given a simplified diet, lacking a still unidentified factor present in certain vegetable oils (Diet 108) extensive malacic lesions of the brain are produced.[1-4] The same diet fed to ducklings does not affect the brain, but leads to widespread degeneration of the skeletal muscles.[5] Pigeons appear to be refractory. We have recently found that the same diet given to turkey poults produces selective necrosis of the smooth muscle of the gizzard wall, unaccompanied by significant lesions in other or-

[5] Levaditi, C., and Nicolau, S., *Compt. rend. Soc. de Biol.*, 1922, **87**, 498; *Ann. Inst. Pasteur*, 1923, **37**, 443; Rivers, T. M., and Pearce, L., *J. Exp. Med.*, 1925, **42**, 523; Berry, G., and Syverton, G. P., *J. Bact.*, 1936, **32**, 356; Levaditi, C., and Haber, P., *Compt. rend. Acad. d. Sc.*, 1936, **202**, 2018.

[1] Pappenheimer, A. M., and Goettsch, M., *J. Exp. Med.*, 1931, **53**, 11.

[2] Pappenheimer, A. M., and Goettsch, M., *J. Exp. Med.*, 1931, **54**, 399.

[3] Pappenheimer, A. M., and Goettsch, M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 177.

[4] Goettsch, M., and Pappenheimer, A. M., *J. B. C.*, 1936, **114**, 673.

[5] Pappenheimer, A. M., and Goettsch, M., *J. Exp. Med.*, 1934, **57**, 35.