appeared on the skin of the mother where virus had come into contact with it on withdrawing the needle. The experiment was repeated in another animal with identical results: no papillomatous or other progressive growths resulted when 25-day embryo skin, secured after hysterectomy and exposed to the virus *in vitro* was implanted into the muscles and subcutaneous tissue of the mother. In previous tests it had been found that implanted embryo epithelium survives and proliferates for several weeks before disappearing.

The results of several collateral experiments emphasize the significance of these tests. Minced portions of normal skin procured from 8 adult, domestic rabbits were exposed *in vitro* to the virus in the same way as was the embryo skin, and auto-implantations of the minced skin were made as before into the muscles and subcutaneous tissues. In every case papillomatous growths developed which were precisely like those resulting from auto-implantation of the Shope papilloma. On the other hand, attempts to infect Brown-Pearce tumor cells with papilloma virus by the same procedure yielded negative results.[5]

Summary. It is plain that the Shope papilloma virus is remarkably specific in its action, affecting only the epidermis of rabbits and hares and failing to influence embryonic epidermis or other kinds of epithelium, even when this is keratinizing as the result of avitaminosis A, or proliferating in consequence of Scharlach R stimulation.

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A Virus Causing Oral Papillomatosis in Rabbits.

ROBERT J. PARSONS AND JOHN G. KIDD. (Introduced by Peyton Rous.)

From the Laboratories of the Rockefeller Institute for Medical Research, New York.

Papillomas can often be found in the mouths of domestic rabbits. They are usually situated on the under surface of the tongue, rarely elsewhere on the buccal mucous membrane. We have found them in 67 (17.4%) of 385 gray-brown, Dutch-belted, New Zealand, Havana and chinchilla rabbits obtained from various local sources. None was present in 44 Kansas cottontails.

[5] Kidd, J. G., Beard, J. W., and Rous, P., *J. Exp. Med.*, 1936, **64**, 79.

The growths occur as discrete, sessile or pedunculated, rugose, filiform or fungiform projections. They are usually multiple, often numerous, and their translucent, gray-white color contrasts sharply with the pink mucosa. They may be 5 mm. across and 4 mm. high, though usually less than half this size.

Microscopically the papillomas consist of folded and greatly thickened epithelium supported upon narrow connective tissue cores. Some coarse branching of the cores is present in the larger growths. Invasion of the underlying structures has not been observed. Mitoses are very frequent in the affected epithelium and both cells and nuclei are abnormally large. No stratum granulosum can be discerned and the cells desquamate when but slightly flattened, and while their nuclei are still notably basophilic. There is a noteworthy absence of inflammatory changes in the supporting connective tissue. No definite inclusion bodies have been found on search. In most animals the growths have retrogressed after some weeks but in some they have persisted unchanged, in one instance for 145 days—the maximum period of observation.

The disease can readily be transmitted by means of Tyrode extracts of fresh, glycerinated, or frozen and dried papillomas. Tattoo inoculation of such extracts into the under surface of the tongues of 59 domestic rabbits has yielded growths in 48 individuals, while all of 32 western cottontails have proved susceptible. Preservation of the papilloma tissue in 50% glycerol for 84 days, as also drying it in the frozen state, has entailed no perceptible loss in its potency.

Filtered extracts of fresh or glycerinated papillomas have regularly proved capable of causing the disease in series after passage through Berkefeld V and N candles. For example, glycerinated papillomas which had been obtained from the tongues of 18 domestic rabbits, were trimmed, pooled and ground in a mortar with sterile sand. Tyrode's solution was added to make a 2% suspension. The clear supernatant fluid obtained after light centrifugalization of this suspension was passed through a Berkefeld V candle which was tested concurrently with *B. prodigiosus*. The culturally sterile filtrate was tattooed into the under surface of the tongues of 7 domestic and 3 cottontail rabbits. By the nineteenth day papillomas had appeared in all the cottontails and in 6 of the domestic rabbits. After 31 days the papillomas from 2 of the cottontails and 1 of the domestic rabbits were pooled and treated as above. The bacteriologically sterile fluid procured by passing the Tyrode suspension through a Berkefeld V candle induced growths in all of the 5 domestic rabbits inoculated therewith.

Control inoculations of the buccal mucous membrane with sterile Tyrode's solution or with Shope papilloma virus in domestic rabbits and cottontails have not produced papillomas.

In general, papillomas have appeared from 9 to 38 days after inoculation, the incubation period varying with the concentration of the inoculum. The experimentally induced growths are usually confluent or semi-confluent along the lines of inoculation, as would follow from the method employed. They are otherwise precisely like the naturally occurring growths. If the neighboring mucosa has been accidentally traumatized during inoculation, papillomas may appear here as well.

The agent causing the papillomas shows a remarkable tissue affinity, regularly inducing growths on the under surface of the tongue but rarely where introduced on the dorsum of the organ or on the floor of the mouth, and never, thus far, when inoculated on the mucous membrane of the nose, conjunctiva, genitals, or the skin of the lip and abdomen. Inoculation of the active agent into the oral mucous membrane of dogs, guinea pigs, rats and mice resulted in no lesions.

Animals carrying the papillomas or in which they have recently retrogressed, generally prove insusceptible on inoculation with potent papilloma extracts. Cottontails carrying the Shope papilloma or proving resistant on inoculation with the virus responsible for these growths invariably prove susceptible to oral papillomatosis on experimental inoculation, but some domestic rabbits have proved resistant, the proportion being no greater, however, than in hosts previously unexposed to the Shope virus.

Summary. Oral papillomatosis is common in domestic rabbits bred in the New York area. The disease is due to an hitherto undescribed virus which is evidently pathogenic for the oral mucous membrane only.