of virus had been employed in testing the resistance to infection, is hard to say. There is, however, nothing in these results to suggest that this might have been the case.

Other than a slight degree of leucocytic infiltration the olfactory mucosae from theelin-treated animals showed no structural features which failed to fall in with variations met with in "normal" olfactory mucosae. While individual mucosae in Group 1 showed epithelia which were above average in thickness, others obtained from animals treated about as long with theelin, showed epithelia which were distinctly below average. There was no evidence of unusual proliferative activity. In 2 mucosae there was evidence of some antemortem detachment of epithelial cells. Whether there is normally some detachment of the olfactory epithelial cells with relation to the menstrual cycle remains a question. In a later paper, in which we shall deal with variations in the olfactory mucosae of normal monkeys, reference will be made to observations suggesting that the olfactory epithelium is not infrequently called upon to repair losses due to natural causes.

The group (Group 2) tested for resistance to poliomyelitis virus showed about the same degree of round cell infiltration along the olfactory pathway[4] as was present in the untreated control group.

What impressed us most in the results of this experiment was the striking response of the sexual skin to the intranasal instillation of estrogen, confirming an already recognized fact that physiologically active drugs are readily absorbed from the nasal mucosa.

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Failure of Sulfanilamide in Treatment of Experimental Vaccinia Rabbits.

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McCammon[1] reported that the early administration of sulfanilamide to 4 cases of benign smallpox appeared to have a beneficial

[4] Sabin, A. B., and Olitsky, P. K., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 300; *J. A. M. A.*, 1937, **108**, 21.

[1] McCammon, W. O., *J. A. M. A.*, 1939, **112**, 1936.

effect upon the disease. In the same year Pierna[2] reported on the treatment of 7 cases with the compound and since vesiculo-pustular evolution of the lesions, desiccation and peeling were accomplished in less than half the time observed in untreated controls, thought that sulfanilamide may attenuate the virus of smallpox and prove specific in the treatment of the disease.

Since cowpox virus is biologically closely related to smallpox virus, we thought it advisable to study the effects of sulfanilamide upon experimental vaccinia of rabbits in order to determine more definitely whether or not the compound had any appreciable clinical effects upon the virus and the lesions produced by cutaneous inoculation. To the best of our knowledge no previous investigations have been reported and we may state at the outset that sulfanilamide has proven ineffective. It may be, however, that the compound is helpful in the treatment of smallpox and likewise in generalized vaccinia of human beings by reducing the degree of secondary infection of vesicles with staphylococci and streptococci from the skin, but since sulfanilamide has had no apparent effect upon experimental vaccinia of rabbits, we believe it quite unlikely to be effective in the treatment of smallpox insofar as infection with the virus is concerned.

Twenty-four rabbits, weighing from 1950 to 2300 g, were employed. The abdomen of each was shaved, the skin scarified and inoculated with seed virus* in the usual manner. Papular lesions were apparent within 48 hours after inoculation with vesiculation on or about the fifth day. Regression began on the seventh to eighth days with healing on the twelfth to fourteenth days. None of the rabbits succumbed.

At intervals of 24, 48, 72, 96 hours and 5 days after inoculation treatment was started, 4 rabbits being used at each interval with 4 untreated controls. Sulfanilamide was administered orally in dose of 0.1 g per kilo, 2 doses being given daily (10 A.M. and 4 P.M.) amounting to 0.2 g per kilo per day and equivalent to 12 g daily per 60 kilo, or approximately 132 pounds of body weight. Each animal received from 10 to 14 doses.

That the compound was absorbed is indicated by the fact that the blood concentrations of free sulfanilamide 4 hours after the first dose varied from 0.7 to 1.8 mg per 100 cc; about 1.5 mg after the third dose and 1.0 to 2.2 mg after the fifth dose. Two hours after the fifth dose the concentration varied from 2.0 to 3.2 mg; 1.48 to 2.16 after the seventh dose; 2.16 to 2.4 mg after the ninth dose;

2 Pierna, S., *Rev. Espãn. de Med. y. Cir. de Guerra, Valladolid*, 1939, **3**, 279.

* Kindly furnished by the Sharp & Dohme Laboratories, Glenolden, Pa.

3.0 to 3.6 mg after the eleventh dose and 2.96 to 3.0 mg after the thirteenth dose.

The results were entirely negative as the compound in the dosage administered was without apparent effect upon the evolution and course of the vaccinal lesions.

Conclusions. 1. Sulfanilamide by oral administration in dosage of 0.1 g per kilo of weight, twice daily for 10 to 14 doses, had no appreciable effect upon the evolution and clinical course of experimental vaccinia of rabbits. 2. Under the circumstances it is unlikely that sulfanilamide has any effect upon the virus of smallpox, although its administration may be helpful in the treatment of smallpox and generalized vaccinia by reducing secondary staphylococcus or streptococcus infections of the vesicles.

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Cultivation of Influenza A Virus in Roller Tubes.

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The prolonged cultivation of vaccinia in roller tube cultures of chick embryonic tissue has been reported.[1] After an initial rise, individual cultures were observed to maintain a high titer of virus for as long as nine weeks. The present communication presents the results obtained in the cultivation of influenza A virus by means of the same method.

The Melbourne strain of influenza A virus which had been passed exclusively in eggs or in chick embryo tissue culture for more than 300 transfers was used. Introduced intranasally 0.05 cc of a suspension of infected embryo diluted 10^{-4} or 10^{-5} in infusion broth killed all mice. Cultures were inaugurated by mixing a suspension of virus with finely minced, 10-day chick embryo (head removed). About 0.6 cc of infected tissue was distributed over the layer of chicken plasma on the inner surface of the lower half of a roller tube. Nutrient fluid consisted of 1.6 cc of so-called 7-2-1 mixture (Simms' solution 7 parts, chick embryo extract 2 parts, chicken serum 1 part). This fluid was changed daily when 20 cc of sterile

[1] Feller, A. E., Enders, J. F., and Weller, T. H., *J. Exp. Med.*, 1940, **72**, 367.