

to infection, 2 showed a questionable rise in temperature and 3 failed to react to the virus. The advent of poliomyelitis after sub-infective intravenous doses of virus when nerves are sectioned adds support to the existence of an insulatory mechanism between the nervous system and the blood.

Normally well isolated from the rest of the body,³ nervous tissue is protected from noxious agents in the vascular system. Trauma to the nervous system, either central or peripheral, breaks down the mechanism regulating the exchange of substances between neural and somatic tissues, and permits the virus to parasitize susceptible nerve cells.

We⁷ have previously shown that sectioning the olfactory tracts prevents infection from the blood stream, even when large intravenous doses of virus are injected. Since intranasally instilled virus is highly successful in infecting monkeys and intravenous inoculation with small doses of virus unsuccessful unless neural tissue is damaged, we interpret the results of the experiments recorded at this time as further evidence that poliomyelitis virus passes directly from the nasopharynx to the brain via the olfactory tracts.

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Effect of Large Doses of Progesterone in the Female Rat.

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In a previous communication we drew attention to the fact that large doses of œstrone markedly enlarge the pituitary, the adrenals and the corpora lutea in the rat.¹ The mammary glands were also greatly developed, but this development was seen only in the normal and not in the hypophysectomized rat. More recently, our findings have been confirmed by Reece, Turner and Hill,² although

⁷ Lennette, E. H., and Hudson, N. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1444.

¹ Selye, H., Collip, J. B., and Thomson, D. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1377.

² Reece, R. P., Turner, C. W., and Hill, R. T., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 204.

other investigators claimed to have obtained mammary^{3, 4, 5} or at least nipple⁶ proliferation with œstrin in hypophysectomized animals. Freud and de Jongh⁷ state that the mammary effect of œstrin is greatly synergized by simultaneous administration of progesterone, both in the normal and the hypophysectomized rat. Since the corpus luteum hormone is generally looked upon as one of the most important factors in the development of the mammary gland, we were surprised to see that simultaneous administration of progesterone and œstrone to ovariectomized rats did not lead to more marked mammary proliferation than would have been elicited by œstrone alone.⁸

In connection with these earlier experiments, it seemed of interest to study whether large doses of synthetic corpus luteum hormone would have an effect upon ovaries, adrenals and pituitary similar to that previously observed with œstrone. Six normally cyclic 5-month-old female rats were injected with 4 mg. of synthetic corpus luteum hormone in corn oil subcutaneously for a period of 12 days. At autopsy on the 13th day, it was observed that their ovaries were subnormal in size, averaging 30 mg. as compared with 39 mg. in the controls. Histological examination showed the absence of any recent corpora lutea or mature follicles. The pituitaries weighed on an average 13.5 mg. as compared with 10.5 mg. in the normal. Histologically, the most outstanding change was the presence of a great number of small cells with relatively dense chromatin. The adrenals did not differ significantly either in weight or in histological appearance from the controls. The thymus was smaller in the injected animals (average 110 mg.) than in the controls (average 205 mg.). The mammary gland was quite undeveloped and differed in no way from that of a normal, untreated animal. The vagina was not cornified and not mucified, only here and there did the epithelium include small cysts filled with mucin. This explains why the vaginal smears became dioestrous within 2 days after the first injection, and remained dioestrous throughout the experiment. The endometrium was dioestrous in type, not frankly progestational.

³ Ruinen, F. H., *Acta Brev. Neerl. Physiol.*, 1932, **2**, 161.

⁴ Asdell, S. A., and Seidenstein, H. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 931.

⁵ Nelson, W. O., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 222.

⁶ Lyons, W. R., and Pencharz, R. I., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **33**, 589.

⁷ Freud, J., and de Jongh, S. E., *Acta Brev. Neerl. Physiol.*, 1935, **5**, 47.

⁸ Selye, H., Browne, J. S. L., and Collip, J. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 198.

While previous experiments on ovariectomized animals⁷ showed that the simultaneous administration of œstrin plus corpus luteum hormone causes mucification of the vagina and progestational proliferation of the endometrium, the present experiments indicate that progesterone alone has no effect on the vagina itself. The diœstrous condition of the vagina observed after progesterone is more likely to be the sequence of the ovarian atrophy caused by this hormone.

Summary. Daily administration of 4 mg. of synthetic progesterone to normally cyclic female rats causes immediate cessation of cycles, without vaginal mucification. There was ovarian atrophy, hypertrophy of the pituitary, and slight atrophy of the thymus. It has no effect whatsoever upon the condition of the mammary gland. Since œstrin is also without any direct effect upon the mammary gland (as shown in hypophysectomized animals) the effect of ovarian hormones on the mamma must be largely dependent upon the presence of pituitary secretions.

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A New Approach to the Therapeusis of Hemolytic Streptococcal Infections.

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The approach to this problem has had as its objective the *in vivo* transformation of virulent organisms into their avirulent phases as indicated previously.¹ Such objective became a possibility following our demonstration in 1915-17² (and later) that streptococci may have pleomorphic granular bacilli as at least one of their avirulent dissociants. The isolation of such strains from blood-cultures of untreated patients convalescent from streptococcal infections lent support to the above working-hypothesis.³ It suggests, perhaps, a natural tendency on the part of the host to combat the parasite by dissociating it into a less virulent, or perhaps into an innocuous form.

¹ Mellon, R. R., and Cooper, F. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 451.

² Mellon, R. R., *J. Bact.*, 1917, **2**, Nos. 2, 3, 4.

³ Koch, K. R., and Mellon, R. R., *J. Bact.*, 1930, **19**, 25.