The presence of fresh corpora lutea following injections was determined by microscopical examination of the ovaries. In the group injected at 17 days, fresh corpora lutea were seen in all cases except the 2 animals previously mentioned. In the group injected at 11 days, ovaries of only 3 animals were examined 4 days following injection at which time fresh corpora lutea were readily identified.

The striking difference in the course and outcome of pregnancy, depending upon the stage of gestation at which ovulation is induced, is indicative of the rate at which changes occur in the hormonal mechanism by which intrauterine life is maintained.

Summary. Ovulation was induced during pregnancy by a single intravenous injection of 10 rat units of pregnancy urine extract. Abortion commonly occurred in rabbits injected about the middle of pregnancy. On the other hand, in animals injected at the beginning of the second trimester, interruption of gestation did not occur.

10701

Viral Effect Produced by Intestinal Contents of Normal Mice and of Those Having Spontaneous Encephalomyelitis.

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Spontaneous encephalomyelitis of mice was first described by Theiler[1] as a new viral disease. The case incidence among stock Rockefeller Institute mice was shown to be 1 or 2 per 1,000[2] and its existence in Germany[3] and in Japan[4] was reported later. Interest in the malady lies in its similarity in many characters to poliomyelitis[1, 4], especially in size of the virus; in its action chiefly on the CNS and the naturally occurring characteristic flaccid paralysis, and in the pathological changes of the CNS. It has been called "poliomyelitis of mice," although Theiler[1] first demonstrated that there is no relationship between the two in host-susceptibilities and immunological reactions.

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1 Theiler, M., *Science*, 1934, **80**, 122; *J. Exp. Med.*, 1937, **65**, 705.

2 Sabin, A. B., and Olitsky, P. K., *J. Exp. Med.*, 1938, **67**, 201.

3 Gildemeister, E., and Ahlfeld, I., *Cent. Bakt.*, I Abt., Orig., 1938, **142**, 144.

4 Iguchi, M., *Kitasato Arch. Exp. Med.*, 1939, **16**, 56.

In view of the recent discussion on the presence of virus in the feces in poliomyelitis, it was thought desirable to study the intestinal contents of mice having the Theiler disease-syndrome and of normal mice. One of 5 stock, "normal" mice caged together exhibited circling. After 4 days it was killed† and its brain and intestinal tract were removed. 0.03 cc of 10% broth suspension of the brain was injected intracerebrally into each of 4 mice, none of which developed disease. The intestines along with their contents were ground, and 1.75 g diluted with 14 cc broth. This was spun at 2500 rpm for 10 minutes and the supernatant filtered through a Berkefeld "V" candle. One of 4 mice injected intracerebrally with the filtrate developed, after 12 days, flaccid paralysis of both posterior extremities and of the lumbar muscles, and showed the usual signs of Theiler's disease. The transfer from this mouse and later passages to the 6th are tabulated. Further transfers are still being successfully carried out.

The source of material for these positive transmissions was a

TABLE I.

Serial Passages (to 6th Transfer) of Unfiltered Brain or Filtered Intestinal Material. Each mouse given 0.03 cc intracerebrally.

Passage	Mouse No. and history	Material tested	No. of mice used	No. paralyzed
1	1—circling, 4 days	Brain	4	0
		Intestines + contents	4	1
2	2-16—paralyzed, 2 days	Brain	4	4
3	2-21 " 2 "	Brain	6	6
	2-22 " 2 " (pooled)	Intestines + contents	5	3
4	2-25 " 1 "	Brain	6	5
	2-39 " 1 " (pooled)	Intestines + contents	8	4
5	2-45 " 2 "	Brain	4	2
		Intestines + contents	6	6
	2-46 " 7 "	Brain	4	3
	2-47 " 7 " (pooled)	Intestines + contents	6	3
6	2-59 " 3 "	Brain	4	1
		Intestinal contents alone	8	4
	2-63 " 3 " (pooled)	Intestinal walls	8	0

† The lethal agent was ether; in operative procedures ether anesthesia was used.

mouse with an indefinite sign, *i. e.*, circling, but no paralyses or other disabilities. The next experiment was performed with the pooled brains, and pooled intestinal contents of 3 animals showing flaccid paralysis for 1 to 2 days. These mice represented the 2nd intracerebral passage of brain tissue derived from the naturally occurring, spontaneous disease. Here again the brain and the intestinal contents injected intracerebrally in normal mice induced the characteristic encephalomyelitis.

The lesions produced in the CNS by injection of filtered intestinal contents derived from both of the passage series are similar to those seen in the natural, spontaneous disease:[1] Neuronal necrosis and neuronophagia, especially marked in the cord, associated with typical perivascular infiltration and with little or no meningeal reaction. Moreover, mice which have recovered from the acute stages of the disease induced by intracerebral passage of brain derived originally from the malady in nature, are resistant to intracerebral inoculation of the "intestinal" active agent. Conversely, the majority of those which have failed to react to the latter are refractory to similar injection of brain obtained from the passaged natural disease.

Further experiments carried out to this time (in 1 or 2 tests comprising 8 to 10 mice in each) indicate that suspensions of intestinal walls washed completely free of their contents, mesenteric glands, salivary glands, and nasal mucosæ, derived from mice in the early stages of the affection produced by intracerebral inoculation of intestinal contents, fail to produce encephalomyelitis. In addition, suspensions of intestinal contents which were active when given intracerebrally exhibited no disease-producing effect when injected subcutaneously (abdominal area) nor sub- and intracutaneously (plantar tissue), and feeding the suspensions through a stomach-catheter or cannibalism of infected mouse-brain also failed to cause illness. Nor did animals reveal the disease when their plantæ were repeatedly scarified while kept in close contact with those in the active stages of encephalomyelitis. The purpose of these preliminary experiments was to elucidate, if possible, the way in which the virus might spread among mice and the relation thereto of the active agent in the intestinal contents, especially since the latter was, at times, as effectively disease-producing by intracerebral injection as were the brain and cord of infected animals.

Attention was then directed to a study of the intestinal contents of normal mice. It was found that the pooled brains of 6 stock mice (of the same age as those used heretofore, namely 30 days of age) showed, after intracerebral inoculation, no viral effect in 6

fresh mice, but the filtered pooled intestinal contents of the same stock animals, similarly inoculated, induced in 6 of 8 mice the characteristic encephalomyelitis. Intracerebral passage of the brain and filtered intestinal contents of the latter was again positive. It would now appear that (a) either normal mice harbor this virus in the intestinal contents, or (b) these contents of mice in general are non-viral but can activate, after intracerebral inoculation of filtrates, a latent carriage of virus, thereby inducing clinically apparent disease. If this occurs, one may postulate that the first test-mouse which reacted to inoculation of the filtered intestinal contents and thus initiated the present series of transmissions may have had its infection brought about in this way. Other substances introduced into the brain of mice do not, as a rule, cause this effect in view of the extremely low incidence of the malady observed among thousands of mice used in this laboratory for experimental transmission of various agents.[2]

10702

Observations on the Mode of Action of Sulfapyridine on Pneumococcus.*

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The introduction of successful chemotherapeutic measures against infection gives rise to speculations as to the mode of action involved. Whitby[1] reported on the effectiveness of sulfapyridine against certain types of the pneumococci and stated that "It appears to exert a definite action on the capsule of the pneumococcus." This view has not been accepted by those who have worked extensively with the drug, although the conception that the capsule is injured in some way, so that typing is either not possible or is rendered difficult after administration of sulfapyridine, has been retained by some clinicians.

Long[2] and his associates have expressed the view that the drug

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1 Whitby, L. E. H., *Lancet*, 1938, **1**, 1210.

2 Long, P. H., Bliss, E. A., and Feinstone, W. H., *Penn. Med. J.*, 1939, **42**, 483.