

6. A new hypothesis is discussed in which it is postulated that motor nerve endings at rest are in part responsible for the removal

of acetylcholine at the neuromuscular junction.

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"Spontaneous" Ovulation in the Rabbit Following Combined Estrogen-Progesterone Treatment. (17848)

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Unlike the human and a large majority of other mammals, the rabbit seldom, if ever, ovulates spontaneously; normally ovulation occurs only after neurogenic stimulation of the hypophysis attendant on coitus. Estrogen has been reported to facilitate the release of ovulating hormone from the rabbit hypophysis in response to copper salts(1), to coitus during pseudopregnancy(2), and to mechanical stimulation of the vagina(3), but progesterone has always been considered inhibitory to ovulation in this species(4,5). In such widely unrelated spontaneously-ovulating forms as the rat(6,7,8) the hen(9) and probably the monkey(10), however, ovulation has been stimulated by the appropriately timed injection of progesterone. Everett(11) has suggested that once the critical factor of timing is understood, progesterone facilitation of LH release may be disclosed in other

species. We have recently found that progesterone administration, independently of extrinsic estrogen, conditions the estrous rabbit in such a way that mechanical stimulation of the vagina induces ovulation(12). The present work reveals that, in a significant number of rabbits, combined treatment with estrogen and progesterone dispenses with the requirement of a coital stimulus and allows ovulation to occur "spontaneously."

This preliminary study employed 30 mature female rabbits, all apparently in estrus as judged by hyperemia of the vaginal orifice. To avoid the possibility of mechanical stimulation the vagina was not examined after the first hormone injection. The estrogen used was α -estradiol benzoate.* The rabbits were injected subcutaneously on 2 consecutive mornings with doses of 85 μ g estrogen in 0.1 ml peanut oil and/or 2 mg progesterone in 0.2 ml peanut oil. In the animals receiving both hormones the progesterone was administered within 4 hours after the second estrogen injection. The ovaries were examined for ruptured follicles at laparotomy about 48 hours after the last injection.

The results are summarized in Table I. It is apparent that whereas neither estrogen nor progesterone alone was followed by ovulation, 4 out of 10 rabbits ovulated after the combined treatment.

The other species in which progesterone has

1. Dury, A., and Bradbury, J. T., *Am. J. Physiol.*, 1943, v139, 135.
2. Klein, M., *J. Endocrinol.*, 1947, v5, xxv.
3. Sawyer, C. H., *Anat. Rec.*, 1949, v103, 502.
4. Makepeace, A. W., Weinstein, G. L., and Friedman, M. H., *Am. J. Physiol.*, 1937, v119, 512.
5. Friedman, M. H., *Endocrinology*, 1941, v29, 628.
6. Everett, J. W., *Endocrinology*, 1940, v27, 681.
7. Everett, J. W., *Endocrinology*, 1948, v43, 389.
8. Everett, J. W., and Sawyer, C. H., *Endocrinology*, 1949, v45, 581.
9. Rotheild, I., and Fraps, R. M., *Endocrinology*, 1949, v44, 141.
10. Pfeiffer, C. A., *Anat. Rec.*, 1950, v106, 233.
11. Everett, J. W., *Progress in Clinical Endocrinology*, S. Soskin ed., Grune and Stratton, New York, 1950, p. 319.

12. Sawyer, C. H., Everett, J. W., and Markee, J. E., unpublished observations, 1950.

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TABLE I.
Summary of Experimental Results.

No. of rabbits	Avg wt, kg	Treatment		Results		
		Estradiol benzoate μ g	Progesterone mg	Ovulated	Failed to ovulate	% ovulated
10	3.5	2 $\times$ 85	—	0	10	0
10	3.4	—	2	0	10	0
10	3.2	2 $\times$ 85	2	4	6	40

been effective in facilitating ovulation have all been spontaneous ovulators, though at least in the rat a neurogenic timing factor is involved in the LH-release mechanism (13,14,8). The rabbit is the first form in which, to our knowledge, a species normally requiring a coital stimulus has been converted to a "spontaneously ovulating" type by hormone administration. In this respect it resembles the persistent-estrous rat, in which spontaneous ovulation can be restored by

13. Sawyer, C. H., Everett, J. W., and Markee, J. E., *Endocrinology*, 1949, v44, 218.

14. Everett, J. W., Sawyer, C. H., and Markee, J. E., *Endocrinology*, 1949, v44, 234.

progesterone treatment(6). To what extent in the rabbit progesterone operates through nervous mechanisms requires further study. Addition of this animal to the growing list of species in which progesterone stimulates ovulation, increases the likelihood that progesterone facilitation may be a fairly general phenomenon.

Summary. Following treatment with estrogen and progesterone 4/10 rabbits ovulated spontaneously, *i.e.*, without the coital stimulus normally required to induce LH release from the hypophysis in this species.

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Effect of Cortisone on Some Reactions of Hypersensitivity in Laboratory Animals.* (17849)

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The effects of ACTH and cortisone which have been reported in the case of a number of different disease states known or thought to involve hypersensitivity of tissues(1-3)

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1. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F., *Proc. Staff Meet. Mayo Clinic*, 1949, v24, 181.

2. Hench, P. S., Slocumb, C. H., Barnes, A. R., Smith, H. L., Polley, H. F., and Kendall, E. C., *Proc. Staff Meet. Mayo Clinic*, 1949, v24, 277.

3. Mote, J. R. (Editor), *Proc. First Clinical ACTH Conference*, The Blakiston Company, 1950.

have suggested that these agents may influence the manifestations of antigen-antibody reactions *in vivo* or of bacterial hypersensitivity. Accordingly, a study was instituted of the effect of cortisone on a number of these reactions of immunity and hypersensitivity in experimental animals.

Procedure. 1. *Effect of cortisone treatment on the tuberculin skin reaction in sensitized rabbits and guinea pigs.* a. A total of 18 rabbits of approximately 2.2 kg were infected intradermally with 0.15 mg of tubercle bacilli (BCG). After 3 weeks it was established that cutaneous sensitivity to tuberculin (OT) and to cytoplasmic particles (CP)