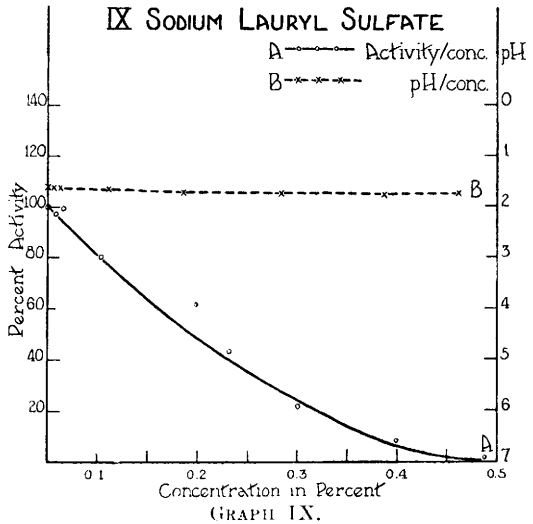

GRAPH IX.

This shows how sodium lauryl sulfate decreases peptic activity without any alteration in pH. Note effectiveness of dilute concentrations.

nesium trisilicate, and mucin inhibited peptic activity by altering the pH, the percent of inhibition being directly related to change in pH. 2. Of these 4, magnesium trisilicate was the most effective inhibiting agent, exerting the greatest effect on the pH. 3. Of the substances used, sodium lauryl sulfate alone completely inhibited peptic activity without any alteration in pH.

13781

Forced Ovulation of Normal Ovarian Follicles in the Domestic Fowl.

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The induction of multiple ovulation following intravenous injection of a luteinizing preparation into hens pretreated with pregnant mares' serum administered subcutaneously for 6 to 100 days has been described.[1] The results set forth in this paper show that ovulation of normally maturing follicles can be forced by at least 17 hours. While the absolute prematurity of ovulation imposed on

[1] Fraps, R. M., and Riley, G. M., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 253.

the maturing follicle seems perhaps small in comparison with some results on mammalian species, the interval is of striking magnitude relative to the normal interval, 24 to 27 hours, between successive ovulations in laying hens. In the regularly laying hen the time of next expected ovulation as well as the time of induced ovulation[2] can be predicted with relatively high accuracy, contributing greatly to interpretation of results based on ovulation of follicles by even a few hours prematurity.

Time Relations in Normal and Induced Ovulation. Estimation of prematurity of ovulation following experimental treatment was made as follows:

(1) The time of next expected normal oviposition was estimated on the basis of the hen's previous record of lay. One half-hour beyond this time was taken as the time, to within one hour, of next expected normal ovulation.[3, 4, 5]

(2) At autopsy of hens, generally 8 to 11 hours following injection, the position of the ovulated yolk in the oviduct was determined by inspection, and by reference to Warren and Scott's[3] time schedule of progression of the yolk through the oviduct the time of actually induced ovulation was estimated. When ovulated yolks were found in the body cavities of autopsied hens, the time of ovulation was taken as the average time at which ovulation occurred in those hens of the same or of a comparable group with yolks in their oviducts. In general, estimates of time of induced ovulation should be accurate to within ± 0.5 hour.

Having established the time of expected normal ovulation and the time of induced ovulation, prematurity of ovulation was obtained as the difference, expressed in hours, between the actual and the normally expected events. All calculations were made for each hen individually.

Materials and Methods. White Leghorn and Rhode Island hens in their first or second year of production were used in all experiments. Birds of the 2 breeds and ages were so distributed to various experimental groups that reaction differentials arising from these sources were minimized. All hens were kept in individual laying cages under a constant 14-hour light-day for at least 2 weeks before being subjected to experimental treatment. During this period—in

[2] Fraps, R. M., Riley, G. M., and Olsen, M. W., PROC. SOC. EXP. BIOL. AND MED., 1942, **50**, 313.

[3] Warren, D. C., and Scott, H. M., *Poultry Science*, 1935, **14**, 195.

[4] McNally, E. H., and Byerly, T. C., *Poultry Science*, 1936, **15**, 280.

[5] Phillips, R. E., and Warren, D. C., *J. Exp. Zool.*, 1937, **76**, 117.

most instances for a considerably longer time—hourly laying records were maintained from 8:00 a.m. to 4:00 p.m. to provide the data required for estimation of prematurity of induced ovulation.

Four hormone preparations were injected intravenously with effective result. The designations and assay data of these preparations follow:

(1) *LH Preparation.** A luteinizing preparation derived from horse anterior pituitaries, assaying 20 rat seminal vesicle units (Fevold test) per cc, and containing also follicle stimulating hormone in considerable quantities. This is the same preparation previously used in bringing about multiple ovulations in pretreated hens.[1]

(2) *Prephysin* (Chappel Prephysin-veterinary).† Primarily the follicle stimulating principle, but containing also "a relatively small amount of the luteinizing hormone." Assayed in rat units for follicle stimulating hormone: 50 rat units per cc.

(3) *Gonadin* (Gonadin Serum veterinary).‡ The sterile serum of pregnant mares, standardized to contain 50 rat units per cc.

(4) *Anteron.*§ Concentrate of the active gonadotrophic principle of the serum of pregnant mares, standardized in international units, and used in the present experiments at ca. 1200 I.U. per cc diluent.

No attempt was made to reduce the gonadotrophic potencies of the four preparations to a single standard, since this was deemed secondary to the demonstration that each was effective in bringing about premature ovulation of the normally maturing ovarian follicle.

Results. The data presented in Table I show that the rupture of ovarian follicles can be induced by at least 17 hours before normally expected ovulation (Anteron, 1200 units, 10:00 a.m. injections). This is not necessarily the maximum prematurity of follicles in which ovulation can be induced. In one hen injected with LH-Chappel at the 20 unit level two follicles were caused to rupture. One of these was presumably of ca. 27, the other of ca. 4.0 hours prematurity. The weights of the two ovulated yolks were 19.4 and 16.9 g, the order of difference in weights being that expected in ovarian follicles due to ovulate on successive days. On the other hand, the injection of Anteron at the 1200 unit level, a level of submaximal effectiveness in causing ovulation of follicles of 11 hours or more prematurity, did not bring about ovulation of more than a single follicle in any hen injected for effect at almost the same time

* Extract especially prepared by Chappel Laboratories, Rockford, Ill.

† Chappell Laboratories, Rockford, Ill.

‡ Cutter Laboratories, Chicago, Ill.

§ Supplied by courtesy of Schering Corporation, Bloomfield, N.J.

TABLE I.
Ovulation of Single Follicle Following Intravenous Injection of Hormone Preparations into Hens.

Preparation	Quantity, units	Time of injection	Hens			Estimated prematurity	
			Injected, No.	Ovulating, No.	%	Avg hrs	Range hrs
LH (Chappel)	20	11:45 p.m.	7	7*	100	3.48	2.3- 4.1
	20	7:30	3	3	100	8.40	8.3- 8.5
	20	4:00	3	3	100	11.20	10.8-11.7
	8	4:00	4	4	100	10.30	10.8-11.7
	4	4:00	3	3	100	10.30	9.7-10.8
	2	4:00	3†	0†	—	ca.10.0‡	—
Prephysin (Chappel)	100	3- 4:00	3	3	100	11.8	11.2-12.1
	50	3- 4:00	3	2	67	11.0	11.0-11.1
	50	9:00	3	2	67	6.3	5.7- 7.0
Gonadin Serum (Cutter)	150	4- 5:00	10	7	70	10.0	8.8-11.0
	100	4:00	3	2	67	11.8	11.1-13.1
	50	3- 4:00	6	2	33	10.6	9.5-12.7
	50	12:00 midnight	3	2	67	3.5	2.4- 5.6
	40	8:00 p.m.	3	1	33	4.9	4.0- 6.3
	20	8:00	3	0	—	ca.5.0‡	—
	10	8:00	3	0	—	ca.6.0‡	—
Anteron (Schering)	1200	10:00 a.m.	12	3	25	16.94	14.2-17.8
	1200	12:00 noon	12	7	58	14.89	14.1-15.7
	1200	4:00 p.m.	8	7	88	11.14	9.0-13.2
	1200	3:00 a.m.	11	11	100	—0.64	—1.4- 2.9
	400	4:00 p.m.	4	1	25	10.88	10.2-11.6
	120	4:00	4	0	—	ca.10.50‡	—

*Two follicles ovulated in one hen of this group.
†No follicle was ovulable in one hen of this group.
‡These figures represent the approximate time at which ovulation might have been expected at next highest effective injection level.

that normal ovulation was expected (Table I, Anteron, —0.64 hour prematurity).

It should be noted that the negative value of estimated prematurity in this group of hens indicates that in some birds ovulation may have occurred independently of and prior to effect by the injected hormone; the fact that the ovulated yolk was found in almost precisely the same portion of the oviduct in every hen, each autopsied exactly 10 hours after injection, is however sufficient proof of induced ovulation in those hens normally due to ovulate later than was actually recorded.

The effectiveness of injection at submaximal levels is dependent to a high degree upon the maturity of the ovulating follicle. The results obtained following injection of Anteron at the 1200 I.U. level and at differing times before expected normal ovulation (Table I) bring out the relation clearly. A similar relation appears following injection of Gonadin Serum, 50 units inducing ovulation in only 33%

of hens with follicles of 10.6 hours prematurity, but in 67% of hens with follicles of 3.5 hours prematurity.

Comment. The results on forced rupture of the ovarian follicle of the domestic hen under the procedures reported in this paper indicate that consummation of the ovulatory process requires the action of a specific hormone or combination of hormones upon relatively mature follicles. The nature of the effective hormone or combination of hormones will be considered elsewhere. Of more immediate interest is the demonstration, not unexpected, that the effectiveness of ovulatory preparations decreases with increasing prematurity of the ovarian follicle. The data indicate also that the "relative prematurity" of a follicle, as measured by ovulatory response, is in part a function of level of injection of the ovulatory preparation; there appears nevertheless to be a limit beyond which increasing dosages will have no effect. Follicles of not more than 8 or 10 hours prematurity are ovulable in a high degree under the conditions described in this paper. It seems probable, though certainly not proved, that normal ovulation in the fowl is consequent upon the sudden release of an appropriate hormone into the blood stream. This hypothesis is now under investigation.

Summary. Ovulation of the normally growing follicle of the hen's ovary can be induced by as much as 17 hours prior to time of expected normal ovulation by intravenous injection of appropriate hormones. A luteinizing preparation from horse anterior pituitaries effected ovulation of follicles 10 to 11 hours prior to time of normally expected ovulation in 100% of injected hens at a level of 4 rat units (Fevold rat seminal vesicle test). The commercial preparations Prephysin, Gonadin serum and Anteron were effective when administered at sufficiently high levels. At appropriate submaximal injection levels the percentage of ovulating hens decreased with increasing prematurity of the ovarian follicles; this effect is more pronounced in follicles of relatively great prematurity at the time of effect of the injected hormone.