and one pathological semen specimens subjected to electrophoretic analysis. 2. The electrophoretic mobilities of these protein fractions after dialysis are identical with those of the albumin, alpha, beta, and gamma globulins of normal serum. 3. Average values for these components as percentages of the total nondialyzable semen protein are: beta globulin, 39.6; alpha globulin, 21.3; albumin, 19.9; and gamma globulin, 19.1. 4. The protein composition of the one pathological semen studied did not differ from the 4 normal semens.

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Difference in Response of Certain Strains of Rats to Augmentative Gonadotropic Effect.

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The phenomenon of synergism between gonadotropic hormones first reported by Evans, Simpson and Austin[1] has been repeatedly confirmed and has since served as an aid in the estimation of the pituitary follicle-stimulating hormone. The most common synergistic combination is that of human chorionic gonadotropin with pituitary follicle-stimulating preparations. It was surprising, therefore, to find that some anterior pituitary preparations prepared in this laboratory and considered fairly certain to contain follicle-stimulating factor in a relatively pure state, gave no augmented response when combined with prolan. The combinations were tested by the ovarian weight increase in normal immature female rats of the Sherman strain obtained from the Rockland Farms. These rats have been used successfully in this laboratory for the assay of either chorionic gonadotropin (prolan) or the gonadotropin of pregnant mare serum alone. They have been found to give responses comparable to those given by Wistar rats from our own colony. However, the elimination of one factor after another finally led to the conclusion that the insensitivity of the strain of rats being used was the only remaining explanation for our failure to get augmentation in test animals when chorionic gonadotropin was combined with a highly purified follicle-stimulating fraction of the sheep pituitary.

When tested on Sprague-Dawley rats, a follicle-stimulating prepa-

[1] Evans, H. M., Simpson, M. E., and Austin, P. R., *J. Exp. Med.*, 1933, **57**, 545.

ration* gave good augmentation when combined with chorionic gonadotropin. A simultaneous and parallel experiment, using Sherman rats brought out forcibly the contrast between the response of each strain. Results are given in Table I. Obviously the ovarian responses of the Sherman rats are simply additive and show no augmentation. This data is merely an example. Using follicle-stimulating preparations of our own we have produced similar results, and have been able to show suitable augmentation in Wistar rats. Results are shown in Table II.

A difference in sensitivity between strains of rats has been noted previously in regard to the anterior pituitary gonadotropins.[2, 3] When males were used, it was found that Sprague-Dawley rats were many times as sensitive as those of the Long-Evans strain.

TABLE I.
Comparative Responses of Sprague-Dawley and Sherman Rats to the Augmentative Gonadotropic Effect.

		Sherman			Sprague-Dawley		
Material	Dose	Ov. wt mg	Range mg	No. rats	Ov. wt mg	Range mg	No. rats
FSH	4.8 units	25.5	11-67	10	26.8	13-42	10
Prolan	20 I.U.	19.4	14-27	10	28.5	18-40	20
PMS	2.5 I.U.	—	—	—	19	11-27	5
	5 I.U.	—	—	—	22	15-29	10
	10 I.U.	30.8	21-44	8	28	17-36	31
	20 I.U.	70.6	58-94	15	—	—	—
FSH + Prolan	4.8 units						
	20 I.U.	42	14-70	10	112	89-142	10
FSH (4.8 units)	2.5 I.U.	—	—	—	75	57-85	5
+ PMS	5 I.U.	—	—	—	89	65-111	10
	10 I.U.	69.9	45-109	8	113	76-135	11
	20 I.U.	79.5	53-109	8	—	—	—
Controls		9.5	9-10	10	15	14.8-16	10

FSH = Follicle Stimulating Hormone.
PMS = Pregnant Mare Serum Hormone.
Prolan = Chorionic Gonadotropin.
1 Unit of FSH = that amount, ½ of which when given subcutaneously once daily for 3 days to hypophysectomized rats (26-28 days old at operation, 7 to 8 days post-operative interval before injections) causes resumption of follicular growth as evidenced at autopsy 72 hours after onset of injections.

* We are greatly indebted to Dr. H. M. Evans for supplying a purified follicle-stimulating preparation through the courtesy of Dr. H. Jensen.

2 Fevold, H. L., *Protein Hormones of the Pituitary*, Manuscript of N. Y. Acad. of Sci., 1942.

3 Fraenkel-Conrat, H., Simpson, M. E., and Evans, H. M., *Endocrinology*, 1940, **27**, 809.

TABLE II.
Comparative Responses of Sprague-Dawley, Sherman and Wistar Rats to the Augmentative Effect.

		Sherman			Wistar			Sprague-Dawley		
Material	Dose	Ov. wt mg	Range mg	No. rats	Ov. wt mg	Range mg	No. rats	Ov. wt mg	Range mg	No. rats
Control		9.5	9-10	7	12.0	10.6-13.7	14	15.0	14.8-16	10
Prolan	20 I.U.	19.3	14-27	10	24.1	18-31	10	28.5	18-40	20
FSH	2 mg	17.9	11-27	10	19.1	15-25	10	18.6	17-21	10
PMS	10 I.U.	24.8	16-34	10	21.9	16-35	10	27.0	20-31	10
FSH + Prolan	2 mg 20 I.U. 2 mg	49.5	36-67	10	73.0	43-112	10	87.0	67-122	10
FSH + PMS	20 I.U.	55.0	47-67	10	60.0	50-68	5	80.0	55-123	10

FSH = Follicle Stimulating Hormone.
PMS = Pregnant Mare Serum Hormone.
Prolan = Chorionic Gonadotropin.

It is entirely conceivable that a similar difference might be even more pronounced in females even though such a striking difference as we have observed has not been reported as far as we know. It may be that histologic differences between the ovaries of synergistically treated Rockland and Sprague-Dawley rats are not as pronounced as the differences in the gross ovarian appearance and weight. Many assays for the gonadotropic activity of pituitary preparations are conducted on the ovarian weight basis. Since the above results indicate that the ovarian response (weight) depends on the strain of rats employed, results obtained in different laboratories must be compared with care when mixed gonadotropins are assayed.

Summary. A marked difference in the sensitivity of three different strains of rats to the synergistic action of certain gonadotropic hormones has been shown. The three strains, Sprague-Dawley, Wistar and Sherman, give comparable responses to the gonadotropins of pituitary, pregnant mare serum and pregnancy urine when administered singly. Only the Sprague-Dawley and Wistar strains show any augmentative response when purified pituitary follicle-stimulating hormone is given in combination with either chorionic gonadotropin (prolan) or pregnant mare serum hormone.