

productivity in litters sired by irradiated male mice he attributed to lethal genetic alterations in the exposed spermatozoa. Subsequent analysis by Snell of several generations of offspring indicated a high incidence in the sperm of chromosomal aberrations of the type known as translocations. Dominant lethal alterations resulting in abortion of the embryos have also been induced in maize pollen by X-rays and ultraviolet radiation.⁸ No cytologic or embryologic examination of such abortive embryos has as yet been reported.

In conclusion, therefore, it should be emphasized that it is possible to demonstrate one type of dominant lethal effect whereby cells are not impaired in their ability to proliferate while their ability to differentiate is at the same time completely destroyed. The lethal effect, it would appear, is probably due to the absence or deficiency of parts of chromosomes, and therefore of gene loci, necessary for the development of the organism. Important implications arise from these considerations since somatic as well as germ cells may be affected by radiation in a manner similar to that discussed in this paper with resulting proliferative growth unaccompanied by any differentiation.

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Specificity of Fowl and Mammalian Antigonalotropic Sera.*

HERBERT S. KUPPERMAN, C. H. MELLISH[†] AND W. H. MCSHAN.
(Introduced by R. K. Meyer.)

From the Zoological Laboratory, The University of Wisconsin, Madison, Wis.

Numerous investigators have found that the injections of gonadotropic extracts over long periods of time result in the production of a substance in the sera of the treated animals that neutralizes the gonad-stimulating action of the injected extract. The antisera obtained from animals repeatedly injected with gonadotropic preparations from either beef or sheep pituitary glands inhibit not only the extract used in the production of the antisera but also various other gonadotropic extracts, such as human, rat and horse pituitary;

⁸ Stadler, L. J., *Proc. 7th Int. Congress of Genetics*, 1939, 269.

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[†] Present address: Lakeside Laboratories, Milwaukee, Wisconsin.

human pregnancy urine and pregnant mare serum. In addition the aspecific antisera are capable of suppressing the endogenous gonadotropic secretion of the rat, rabbit and dog pituitary. A discussion of these data will be found in recent review papers on antihormones.^{1, 2} A tentative explanation has been offered by Parkes and Rowlands³ to explain the phenomena whereby an antisera for the pituitary gonadotropic hormone from one animal is capable of inhibiting both exogenous gonad-stimulating preparations and endogenous gonadotropic secretion of the pituitary gland from other animals. Their hypothesis states that the gonadotropic complex of extracts when injected into rabbits acts as a haptene and its association with heterologous protein makes it capable of producing aspecific antigonadotropic substances. Parkes and Rowlands³ found, however, that beef antigonadotropic serum although effectively inhibiting gonadotropic secretions and extracts from mammalian pituitaries, serum or urine, is without action against the endogenous gonadotropic secretion of the chicken hypophysis.

In an attempt to obtain more information concerning the specificity of antigonadotropic substances experiments were designed to determine whether antisera developed against the gonad-stimulating hormone of chicken or sheep pituitaries would prevent the gonadotropic effect of mammalian gonadotropins and extracts of chicken pituitary glands.

Procedure. The sheep antigonadotropic sera were obtained from rabbits repeatedly injected with an aqueous, supercentrifuged extract of sheep pituitary glands. The rabbits were injected with 250 mg equivalent of dried powder per day for the first 25 days, after which the same dose was administered every second day for 3 months or longer. The chicken antigonadotropic serum was prepared by injecting an aqueous suspension of 25 mg of air-dried chicken pituitary powder into rabbits every day for the first 25 days, followed by injections of the same dose every second day for 4 months. The blood was obtained by cardiac puncture and the serum prepared by centrifugation.

The inhibitory qualities of the antisera were determined by the ability of the sera to prevent the action of the gonad-stimulating extracts in rats when the serum and the extract were simultaneously administered by separate injections to 21-day-old female rats in 9 equal doses of 0.5 cc during a period of 4.5 days. Autopsy was

¹ Collip, J. B., Selye, H., and Thomson, D. L., *Biol. Rev.*, 1940, **15**, 1.

² Thomson, D. L., Collip, J. B., and Selye, H., *J. A. M. A.*, 1941, **116**, 132.

³ Parkes, A. S., and Rowlands, I. W., *J. Physiol.*, 1937, **90**, 100.

done during the morning of the sixth day and the ovaries of the rats were weighed to the nearest milligram. The aspecificity of the sheep antigonadotropic serum was determined by its inhibitory effect on various gonadotropic extracts other than that made from sheep pituitaries.

Two lots (A and B) of sheep antigonadotropic rabbit serum were used. "A" represents the serum from a single rabbit while "B" is the pooled serum from several rabbits repeatedly injected with sheep pituitary extract. Serum A was injected into rats with the following gonadotropic preparations: aqueous extracts of fresh and acetone-dried sheep pituitaries, suspensions of dried human pituitary glands, suspensions of chicken pituitary glands, pregnant mare serum and an extract of human pregnancy urine made by alcohol precipitation. Serum B was injected with sheep, rat and chicken pituitary extracts and purified pregnant mare serum⁴ and purified human pregnancy urine extract obtained by benzoic acid adsorption.

The chicken antigonadotropic rabbit serum was obtained from one rabbit only and was tested for antigonadotropic action by injecting it with sheep and chicken pituitary gland extracts.

Results and Discussion. The data concerning the inhibitory action of antiserum A and B and antichickens rabbit serum are recorded in Table I. The sheep antigonadotropic rabbit sera were effective in completely neutralizing the gonadotropic activity of the extracts from mammalian sources but were ineffective against the gonad-stimulating action of chicken pituitary glands. The serum of the rabbit repeatedly injected with the suspension of chicken pituitary powder effectively inhibited the action of the gonadotropic hormone of chicken hypophyses, but no demonstrable inhibitory effect could be detected when the chicken antigonadotropic rabbit serum was injected with sheep pituitary extracts.

The gonadotropic effects of the chicken and mammalian preparations are essentially the same when administered to 21-day-old female rats since each produces follicles and corpora lutea.^{5, 6} However, when an antihormone is formed against these extracts, although both produce ovarian growth in mammals, a definite class specificity is noted as regards the neutralizing action of the sera. This relationship of class specificity and order aspecificity of

⁴ Cartland, G. F., and Nelson, J. W., *J. Biol. Chem.*, 1937, **119**, 59.

⁵ Meyer, R. K., Mellish, C. H., and Kupperman, H. S., *J. Pharm. and Exp. Therap.*, 1939, **65**, 104.

⁶ Leonard, S. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **37**, 566.

TABLE I.
Effect of Chicken and Sheep Antihormone on Gonad-stimulating Action of Mammalian and Chicken Gonadotropins.

Gonadotropic substance	Amt	Type of antisera	Dose of antisera, cc	Avg ovarian wt	
				Gonadotropic substance	Gonadotropic substance + antisera
Sheep pituit. ext.	100 mg equivalent of powder	AntiSAP* A	2	69 (6) †	10.5 (4) †
Sheep pituit.—fresh susp. of whole gland	200 mg	" A	2	38 (3)	9.0 (2)
Human pituitary	5 mg air-dried powder	" A	2	42.5 (9)	17.5 (2)
Human pregnancy urine ext.	35 mg powder	" A	2	40 (4)	16.5 (4)
Pregnant mare serum	0.25 cc	" A	2	38 (3)	9.0 (2)
Chicken pit.—fresh susp. of whole gland	200 mg	" A	2	48 (8)	37.5 (8)
Sheep pituit. ext.	100 mg equivalent of powder	" B	1	74 (11)	14 (8)
Purified human pregnancy urine ext.	1 mg powder	" B	2	44 (4)	15 (4)
Purified pregnant mare serum	0.5 mg powder	" B	2	184 (4)	8 (4)
Rat pituitary	2 mg air-dried powder	" B	2	58 (4)	9 (4)
Chicken pituit.	40 mg " " "	" B	2	53 (9)	85.6 (10)
" "	40 mg " " "	" B	2	53 (9)	14 (6)
Sheep pituit. ext.	100 mg equivalent of powder	AntiCAP†	2	85 (4)	102 (5)

*Sheep antigonadotropic rabbit serum.

†Chicken antigonadotropic rabbit serum.

‡Figure in parenthesis indicates the number of rats used.

mammalian and aves antigonadotropic sera is like that found in serological relationships where interclass specificity and interorder aspecificity are noted in the study of classical antigen-antibody reactions. The results reported herein suggest that the gonadotropic complex of chicken hypophysis is immunologically distinct from that observed for the mammalian gland and give further support to the theory that antigonadotropic substances are immune bodies.

Summary. Sheep antigonadotropic rabbit serum, aspecific in nature, although effective in inhibiting the gonadotropic action of extracts of mammalian tissues and fluids did not prevent the typical effect of gonadotropic extracts made from chicken hypophyses. Chicken antigonadotropic rabbit serum, while inhibiting the gonadotropic action of chicken pituitary glands, was ineffective against gonadotropic extracts of sheep pituitary glands. The possible relationship of these experiments are discussed in regard to the nature of the antihormone mechanism.

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Effects of Estrone and Progesterone on Male Rabbit Mammary Glands. I. Varying Doses of Progesterone.

WM. R. LYONS AND DANIEL A. MCGINTY.

From the Division of Anatomy, University of California Medical School, Berkeley, and the Research and Biological Laboratories, Parke, Davis, and Company, Detroit, Mich.

Turner and Frank¹ showed that whereas estrogen caused growth of the duct system and slight lobule proliferation in the male rabbit mammary gland, the combination of estrogen and progestogen caused lobule-alveolar growth simulating that seen in pregnancy. The hormones used were impure, but were assayed for rat units of estrogen and rabbit units of progestogen and judged by the results, were uncontaminated, one with the other. Until recently few investigators have had at their disposal sufficient progesterone with which to investigate this problem further, and, as far as we are aware, the doses of estrone and progesterone that will synergize best to cause optimal mammary growth have not as yet been satisfactorily determined in any animal form. In the preliminary in-

¹ Turner, C. W., and Frank, A. H., *Mo. Agr. Exp. Res. Bull.* 174, 1932.