their infection varied from 22 to 135 days. Both drugs were given in 0.5 g amounts for 6 successive days. Forty-eight hours after the last dose the animals were bled and 3 cc of blood from each monkey was subinoculated intravenously into separate normal monkeys. The blood from the 2 monkeys which received sulfanilamide was not infectious for normal monkeys while the blood from the sulfanilyl sulfanilate treated monkeys produced an infection in the normal animals.

Treatment of avian malaria. Sulfanilamide and sulfanilyl sulfanilate had no prophylactic effect or therapeutic value in the treatment of *P. cathemerium* infections in canaries or *P. lophuræ* infections in young chicks.

Summary. Sulfanilamide was found to have a prophylactic value and a marked therapeutic effect on acute *P. knowlesi* infections in rhesus monkeys. It had, in addition, a direct action upon the parasites *in vitro*.

Sulfanilyl sulfanilate proved an ineffective prophylactic agent; it had no apparent *in vitro* action on the parasites, but some therapeutic value in acute *P. knowlesi* infection was noted.

In chronic infections 3.0 g of sulfanilamide given intraperitoneally was sufficient to render blood non-infectious for susceptible monkeys, while the same amount of sulfanilyl sulfanilate was without effect.

Sulfanilamide and sulfanilyl sulfanilate were ineffective for prophylaxis and had no therapeutic value when tested against infections produced by 2 different species of avian plasmodia.

10011

Effect of Splenectomy on Response to Pituitary Material and the Question of the Antihormone.

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Although there is unanimity among investigators in the field that inhibitory substances appear in the blood following continuous treatment with various endocrine extracts, controversy still exists regarding the nature of these antihormone principles, and the mechanism responsible for their production. This controversy, in general, is confined to two schools of thought. The first adheres to the

idea that antihormones are normally present in the blood of animals in varying amounts, the concentration of which is increased by hormone injection. Collip,[1] for example, compares the hormone-antihormone complex to a buffered system. (For a review of the more pertinent references on this subject, see Gordon.[2]) The other school believes the inhibitory substances are antibodies, evoked because of the association of the injected hormone with foreign protein.

One of the strongest arguments in favor of the antibody-like nature of these antagonistic substances has been the failure of animals receiving treatment with pituitary hormones of the same species to become refractory or develop antihormone substances. This has been demonstrated in different ways by numerous investigators.[3-10] Only Collip and his collaborators[11, 12] have reported refractoriness or inhibitory substances in rats and sheep treated with pituitaries of homozoic animals.

Recently, we[2, 13, 14] have shown that the so-called reticulo-endothelial system, known to be concerned with the production of antibody substances,[15] is intimately related to the state of refractoriness which develops after prolonged treatment with heterozoic endocrine extracts. A short time ago, Emery[16] reported experiments which demonstrated that splenectomy does not alter the ovarian response in rats receiving implants of rat pituitaries. Although this is the result one would expect if the antihormone substances are

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antibody-like, because of the great variation of ovarian weights in Emery's control and experimental groups of animals, we decided to repeat his experiment, using a method which would yield less variable results. At the same time, in order to settle the matter completely, we thought it advisable to conduct another series of experiments to determine whether injections of pituitary material, prepared in the same way, but from a heterozoic source, would produce any different effect in normal as compared to splenectomized animals.

Rat pituitaries were obtained from 135 male animals (150-200 g) castrated approximately 2 months before the experiments were begun. Castration was performed to increase the gonadotropic potency of the glands. On the days of injection, 15 of these animals were killed, the pituitaries removed, and minced with fine scissors to yield a pulp which could be taken up in a small amount of saline for injection purposes. Nineteen control and 19 splenectomized immature (25-30 days old) female rats from the same litters were injected intraperitoneally with 5 mg of this whole rat pituitary material 9 times, the injections being evenly distributed over a period of 25 days.

Sheep pituitaries from freshly slaughtered animals were employed for the second part of the experiment. As with the rat pituitaries, this material was minced up finely and then mixed with a small amount of saline for injection. Ninety mg of whole sheep pituitary prepared in this way, when administered 9 times, was found to have approximately the same effect on the ovarian weight of the immature rat as nine 5 mg injections of the whole castrate rat glands. Twenty normal and 17 splenectomized immature female rats from the same litters were given nine 90 mg intraperitoneal injections, distributed over a period of 25 days. All rats employed in this study were from a highly inbred strain and were free of *Bartonella muris*.

Twenty-six days after beginning treatment all the animals were sacrificed and the ovarian weights determined. Similarly the uteri were cleanly dissected, pressed on a piece of blotting paper to expel any fluid, and the weights measured. The ovarian and uterine weights obtained in these experiments together with a statistical analysis of the results are given in Table I. The ovarian and uterine weights in 12 normal untreated 52-55-day rats are also included.

From an observation of this table, the following conclusions may be reached: (1) Removal of the spleen does not alter the ovarian and uterine weight response to pituitary material from homozoic

TABLE I.
Ovarian weights (mg).

Animal	Pituitary inj.	No. of animals	No. of inject.	Mean ovarian wt. ± S.E.	Range	Mean diff. / S.E. of diff.	Coeff. of variation
Normal	Castrated ♂ rat	19	9	40 ± 2.2	22-58	1.3	23.7
Splenect.	" ♂ "	19	9	36 ± 2.1	24-56		24.7
Normal	Sheep	20	9	34 ± 2.2	20-48	6.4	29.1
Splenect.	"	17	9	52 ± 1.8	39-65		14.2

Uterine weights (mg).

Animal	Pituitary inj.	No. of animals	No. of inject.	Mean uterine wt. ± S.E.	Range	Mean diff. / S.E. of diff.	Coeff. of variation
Normal	Castrated ♂ rat	19	9	112 ± 6.3	66-161	0.89	24.2
Splenect.	" ♂ "	19	9	105 ± 4.8	72-145		19.4
Normal	Sheep	20	9	85 ± 4.6	52-125	6.7	24.2
Splenect.	"	17	9	142 ± 7.2	105-197		20.8

Ovarian and uterine weights (mg) in normal 52-55-day rats.

No. of animals	Mean ovarian wt. ± A.D.	Mean uterine wt. ± A.D.
12	16 ± 2.3	52 ± 10.6

S.E.—Standard Error. A.D.—Avg Deviation.

animals. This may be seen from the values of the standard errors, and the fact that the value of the difference between the means divided by the standard error of the difference between the means is less than 2. This would be in agreement with the conclusions reached by Emery. (2) The statistical analysis, however, reveals that splenectomized rats, injected with pituitary from heterozoic animals, show a greater increase in ovarian and uterine weights than normal rats similarly treated.

These results are in total accord with the general contention that the refractory state which develops after prolonged treatment with heterozoic endocrine material is brought about by a mechanism similar to that responsible for the production of antibodies following injection of antigenic material.

It may be argued that the effects obtained with the sheep pituitary material are due to the greater quantities of sheep as compared to the amounts of castrate rat pituitary injected. As has already been pointed out, however, the sheep and rat material produced approximately the same intensity of effect on the ovarian and uterine weights. That the amount of protein injected does not determine the difference may be seen from some of our earlier experiments[2] which show that great differences in effect in splenectomized and control animals are obtained with the use of small amounts of an endocrine preparation (Follutein) which contains very little protein.

Summary. Splenectomy in rats is without effect on the ovarian and uterine weight response to injections of homozoic pituitary material. Splenectomized rats, however, show greater response when treated with pituitary material from a heterozoic source than similarly treated controls. This lends further support to the contention that the state of refractoriness which develops after prolonged treatment with hormone preparations is immunological in nature.

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Effect of Parathyroid Extract upon Volume of Parathyroid Glands in Normal and Partially Nephrectomized Rats.

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In the course of certain experiments upon sensitiveness of partially nephrectomized rats to parathyroid extract, an opportunity