

10424

Progesterone in Adrenalectomized Rats.

EDWARD L. SCHWABE AND FREDERICK E. EMERY.

From the Departments of Materia Medica and Physiology, University of Buffalo.

Two recent issues of this journal contained reports on the beneficial effect of progesterone in rats following adrenalectomy.^{1, 2} Similar effects had been noted in ferrets,³ in dogs,⁴ and for related compounds in man.⁵ This is not surprising since Rogoff had discussed it as early as 1927⁶ and, more recently, large corpora lutea induced by pituitary implants were found to ameliorate the symptoms of adrenalectomy.^{7, 8, 9} Until last year negative results with progesterone were common. Five of these have been reviewed by Gaunt and Hays⁸ and our attempts to show the value of progesterone were so unsatisfactory that we did not mention them in discussing the rôle of corpora lutea.⁹ We feel confident now that our failures with progesterone were due to inadequate dosage. Until recently the progesterone* we used contained 1/25 mg per cc; now it is available in 5 or even 10 mg per cc. As soon as we increased the dose per rat to one milligram the rats lived.

Female rats were used throughout these experiments. The adrenals were removed in 2 operations at 25 and 30 days of age respectively. Body weights were usually recorded each day. The adrenalectomized controls were litter mates of the injected rats. All animals were kept in a constant temperature room at 80°F and were fed Purina dog chow and water. The injected rats were closely watched for signs of weakness and in only 2 cases was it necessary to give more than the usual dose of 1 mg daily, and in these cases only 2 extra milligrams were needed. Since in both water and oil control groups the majority of rats had succumbed by the 13th day, we

¹ Gaunt, Robert, *et al.*, *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 319.

² Green, R. R., *et al.*, *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 83.

³ Gaunt, Robert, and Hays, H. W., *Am. J. Physiol.*, 1938, **124**, 767.

⁴ Thorn, G. W., and Engle, L. L., *J. Exp. Med.*, 1938, **68**, 299.

⁵ Simpson, S. L., *Lancet*, 1938, **2**, 557.

⁶ Rogoff, J. M., and Stewart, G. N., *Am. J. Physiol.*, 1927, **79**, 508.

⁷ Marrian, F. G., and Butler, G. C., *Ann. Rev. Bio. Chem.*, 1937, **6**, 303.

⁸ Gaunt, Robert, *Symp. Quant. Biol.*, 1937, **5**, 395.

⁹ Emery, F. E., and Schwabe, E. L., *Endoc.*, 1936, **20**, 550.

*We are indebted to Dr. Erwin L. Schwenk of the Schering Corporation for his kindness in supplying us with generous amounts of Proluton, a crystalline, synthetic progesterone in sesame oil.

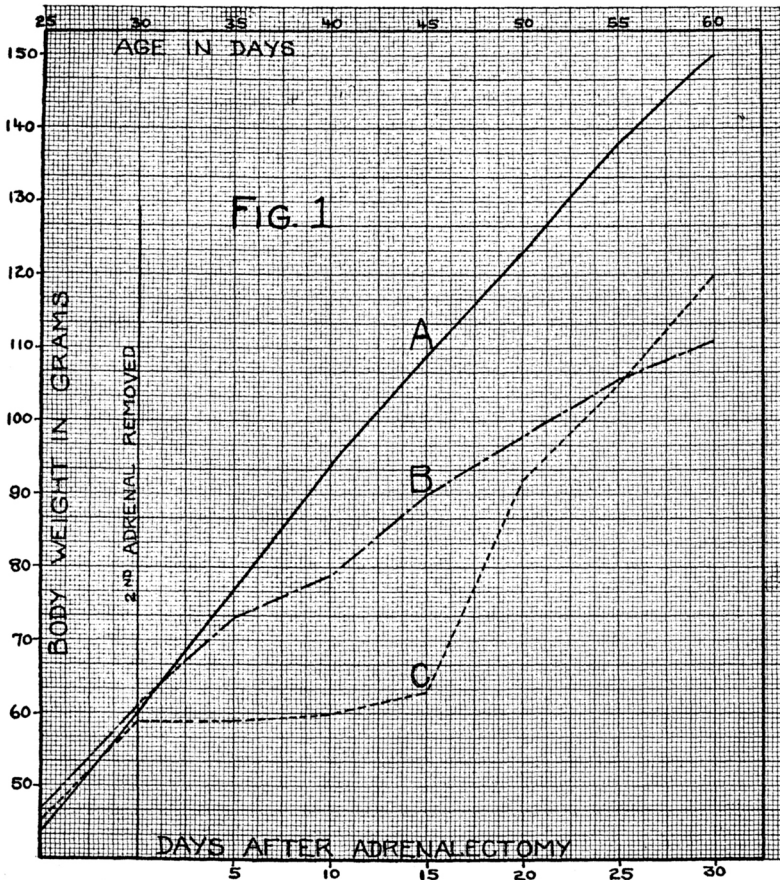


FIG. 1.

Mean body weights are shown for rats from 25 to 60 days of age. A—25 normal females. B—10 adrenalectomized females injected intramuscularly with 1 mg of progesterone daily for 13 days, then 1/5 mg for 7 days. C—30 adrenalectomized female controls.

decided to carry along the progesterone-treated animals with 1/5 mg daily from that date to the 20th day.

This procedure was sufficient to keep the weight curve of the treated animals about midway between the normal and adrenalectomized controls (Fig. 1). Larger amounts of progesterone would probably keep the weights equal to or even above normal, as was found for active corpora lutea induced by pituitary grafts.⁹ All of the rats receiving progesterone lived and gained weight for 20 and more days (Fig. 1). After the injections were stopped, 4 rats died within 5 days and most of the others were not gaining in weight. The fact that hormones in oil are slowly absorbed probably helped to keep these rats going after progesterone was greatly reduced on the

13th day and also after it was discontinued. Estrin in oil is poorly absorbed when injected subcutaneously.¹¹ To avoid this all the injections were made intramuscularly.

The 30 adrenalectomized controls, 10 of which received $\frac{1}{4}$ cc of sesame oil daily, began to die on the seventh day after the second adrenal had been removed. The numbers alive 5, 10, 15, 20, and 25 days post-adrenalectomy were 30, 24, 11, 8, and 7 respectively. Removal of the adrenals in 2 stages was a factor in prolonging life. Also, different colonies of rats differ in the number of animals dying after adrenalectomy.¹⁰ Our colony seems to be more resistant to the effects of adrenalectomy now than it was a few years ago; and our growth curve for normal rats is now greater (Fig. 1) than it was in 1936.⁹

Summary. Our results confirm previous reports that progesterone will keep adrenalectomized rats alive.^{1, 2, 12} In our colony, after 2-stage adrenalectomy, doses of one milligram daily or less were usually adequate to keep young, newly-weaned, female rats alive and showing some gain in weight throughout the treatment period.

10425

Analysis of Present Methods of Collecting Tubercle Bacilli from Urine.*

HARRY A. FELDMAN AND JOHN H. HANKS. (Introduced by Leland W. Parr.)

From the Department of Bacteriology, Hygiene and Preventive Medicine, The George Washington University School of Medicine, Washington, D. C.

In a study on the concentration of tubercle bacilli from urine¹ two standard procedures were used as controls: Petroff's tannic-acid method[†] and direct centrifugation for one hour. Since the detailed

¹⁰ Gaunt, Robert, *Am. J. Physiol.*, 1932, **103**, 494.

¹¹ Deanesly, R., and Parkes, A. S., *J. Physiol.*, 1933, **78**, 155.

¹² Fischer, A., and Engel, M., *Rev. franc. d'endocrin.*, 1938, **16**, 400.

* Aided by a grant from the U. S. Public Health Service.

¹ Hanks, J. H., and Feldman, H. A., to be published.

[†] *Petroff's Tannic Acid Method* (Trudeau Routine Laboratory Procedure):

1. Acidify urine with few drops of 30% acetic acid. To each 1000 cc of urine add 2 cc of 5% tannic acid. Store urine in ice-box 24 hours. Decant supernate and centrifuge sediment for 2 minutes at top speed. (In our experience, centrifugation for 5-10 minutes was required to pack the sediment.)

2. Decant supernate and dissolve sediment with N NaOH. Digest and add H₂O to fill the tube, centrifuge and decant the supernate again. Spread the sediment over clean slides.

3. Add a drop of N HCl and fix the smear with heat.