

protein-fraction from patient's serum plus ultrafiltrate has been found regularly to possess a marked degree of killing power. The constituents individually, however, have not, except for the variations previously discussed, given comparable results. The results suggest, therefore, that the active principle responsible for the destruction of streptococci consists of elements which are separable into inactive individual constituents. However, when mixed together, the streptococidal property becomes effective. Studies at the present time are too incomplete to permit final interpretation of the results just described. Questions concerning the solubility of the protein preparation, or the influence of the concentration of electrolytes, or other possible factors associated with the complex chemical composition of serum require further investigation before the nature of the active principle can be completely defined. From the results so far obtained the significant constituent of ultrafiltrate seems to be neither protein nor ether-soluble lipid.

9463

### Menstruation Inhibiting Action of Testosterone.

CARL G. HARTMAN.

*From the Department of Embryology, Carnegie Institution of Washington, Baltimore.*

The following experiments were performed to test the Androgen Testosterone Ciba for its possible replacement value of progesterone as an inhibitor of the menstrual flow.

1. *Inhibition of menstruation in the normal cycle.*

Monkey No. 245 was selected for this experiment for the great regularity of her menstrual cycles. These ran as follows: 1935-36: 28, 25, 24, 24, 24, 25, 28 days; 1936-37: 26, 25, 25, 26, 25, 26 days. The female was likewise ovulating with regularity and was fertile, a 56-day embryo having been removed by hysterotomy January 9, 1934.

Last menstrual period, March 23, followed by ovulation before April 13 (exact day not known).

Beginning April 13, 10 mg. of testosterone\* was administered

---

\* The author wishes to thank the Ciba Company for the generous supply of Testosterone and Testosterone Propionate placed at the disposal of the laboratory; likewise to E. R. Squibb and Sons for both material and the counsel of J. A. Morrell over a period of years.

daily for 12 days, that is, to April 24 (except that 20 mg. was administered on Saturdays, none on Sundays; in this case 20 mg. was injected on the last day). Menstruation began on April 30. The succeeding cycle was 29 days in length.

Result: In this experiment the menstrual cycle was lengthened to 38 days as against an average of 25 or 26 days, a maximum of 28 days for the spontaneous cycles occurring previous to the experiment.

2. *Inhibition of menstruation after castration.*

Monkey No. 305. Received as mature menstruating female in September, 1934, weighing 4530 gm.

January 17, 1935, day 21 of cycle, ovarian follicle burst under palpating finger; corroborated by laparotomy January 18; menses, January 25; laparotomy January 28, ovary removed. It was found that no corpus luteum had formed.

December 2, 1935, day 8 of cycle, ovarian follicle again burst under palpating finger; laparotomy December 12, biopsy of corpus luteum and endometrium. Corpus luteum was found to be well developed.

December 18, 1936, female gave birth to normal male baby.

Menses occurred February 11, March 6, and March 30, 1937.

On April 15, day 17 of cycle, the remaining ovary was removed. From April 14 to 26 the animal received 10 mg. of free testosterone\* daily as above. She was killed on April 27.

Result: The bleeding which is to be expected within less than 6 days after castration was in this experiment inhibited for 12 days, when the animal was killed.

3. *Inhibition of menstruation after estrin withdrawal.*

(a) Monkey No. 463. This multipara weighed 5540 gm. when she was received in August, 1936. She furnished a slightly pathological 15-day ovum excised by hysterotomy on October 16, when one ovary was also removed. A second but normal 15-day ovum was recovered on December 8 by the same means and the remaining ovary removed. The bleeding which followed the hysterotomy and castration stopped on February 16.

By injection of 100 R.U. daily of Amniotin Squibb\* April 13 to 17, bleeding was effected April 22 to May 3.

The amniotin injection was repeated May 3-7, and from May 8 on 10 mg. Testosterone Propionate Ciba\* was injected daily as above until May 20, that is for 13 days. May 22, 15 days after discontinuance of estrin injection the animal was killed. No bleeding had taken place in this period.

(b) Monkey No. 330, a fertile female, furnished 2 embryos

removed by hysterotomy. Castration was completed at the second operation on December 14, 1936.

In quite an unrelated experiment (mentioned here to complete the animal's history) a course of treatment with amniotin was given from January 18 to February 7, 1937, in gradually decreasing dosages and bleeding occurred February 8-17.

A second bleeding, as a control to the succeeding experiment, was effected May 8-11 by injection of 100 R.U. of amniotin daily from April 23-28. The injection was repeated for 5 days, May 17-21. The bleeding that would have occurred following this last injection was successfully inhibited for 63 days with testosterone propionate injected as above (10 mg. daily). The last injection was made on the sixtieth day, the animal killed 3 days later.

Result: The menstrual bleeding which uniformly occurs in a favorable animal following injection of 500 R.U. of amniotin over a period of 5 days was inhibited for 63 days.

Incidentally it was observed that with the injection of testosterone the vaginal desquamation reaches zero, whereas with estrin it ranges up to 50% of the vaginal lavage. No pregravid transformation of the endometrium is brought about in the monkey (nor in the rabbit) by testosterone. On the other hand the mammary gland proliferates and grows acini in response to the male hormone testosterone and, surprisingly, the sex skin remains almost as red as with estrin injections (Amniotin Squibb or Progynon Sherring), although swelling was not observed with the dosage employed. The phallus was markedly enlarged.

*Conclusion.* Testosterone or Testosterone Propionate inhibits the onset of menstruation in the normally cyclic monkey, after castration and after cessation of estrin injection.

In this sense this androgen simulates the action of progestin, as it does also in its stimulation of mammary development and in its inhibiting action on the vaginal mucosa. In its effect on the sex skin, however, it seems able to replace the estrogens, for this remained brilliantly red in a castrate for 63 days after estrin deprivation.