

# RESEARCH PAPERS

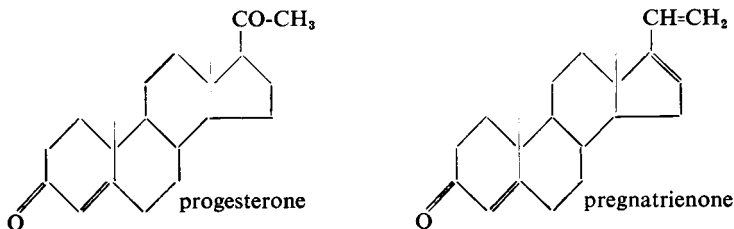
## THE HORMONAL EFFECTS OF PREGNATRIENONE

BY J. M. ROBSON AND A. A. SHARAF

From the Guy's Hospital Medical School

Received October 25, 1950

THE effects of this substance have never been described, and appear to be of some interest. They resemble those produced by progesterone.



**Progestational Proliferation.** A rabbit was ovariectomised and treated with 10  $\mu\text{g}$ . of œstrone per day for 7 days and then with pregnatrienone in oil, over 5 days; a total dose of 25 mg. produced a progestational proliferation of ++ on the McPhail scale. Two rabbits similarly treated with a total of 10 mg. showed no proliferation. The local effect in the rabbit was tested by the method of Höhn and Robson<sup>1</sup> which involves the implantation of the substance as a solid; the smaller doses are given diluted with cholesterol. The results are given in Table I and show

TABLE I  
DEGREE OF PROGESTATIONAL PROLIFERATION PRODUCED BY DIFFERENT IMPLANTS OF PREGNATRIENONE

Dose	1 mg.	0.1 mg.	10 $\mu\text{g}$ .	5 $\mu\text{g}$ .	2 $\mu\text{g}$ .	1 $\mu\text{g}$ .
Effect ... ..	+++	++	++	++	—	—
				+++	++	—
				++	+	—
					++	—

that as small a dose as 2  $\mu\text{g}$ . locally produced some progestational proliferation in 3 out of 4 animals. Progesterone produces an effect under similar conditions in doses of about 1  $\mu\text{g}$ . (Höhn and Robson<sup>1</sup>). Hence the substance is only half as active as progesterone when given locally, but has about 1/25 the activity when given systemically.

**Maintenance of pregnancy.** Mice were ovariectomised on the 10th day of pregnancy (dated from the finding of the vaginal plug). The injections were started on the day before ovariectomy and the substance was given in oil, in two doses, morning and evening. Daily doses up to 4 mg. failed to maintain pregnancy.

**Effects on vagina.** The substance was dissolved in oil or in propylene

## HORMONAL EFFECTS OF PREGNATRIENONE

glycol and injected into ovariectomised mice on the morning and evening of 2 consecutive days. A total dose of 1 mg. produced no effect on the vagina, as indicated by the vaginal smear.

*Inhibition of vaginal action of œstradiol.* This was tested by the method described by Robson<sup>2</sup>. It was found that 4 mg. of pregnatrienone produced no antagonism of the cornifying action of 0.1 µg. of œstradiol, but that that dose of œstradiol was markedly antagonised by 10 mg. of pregnatrienone. Hence this compound has at most 1/10 the activity of progesterone in this respect.

*Effect on the uterine response to sodium œstrone sulphate.* Sodium œstrone sulphate, acting *in vitro*, causes contraction of the œstrous uterus of the mouse, but relaxes the uterus of pregnant mice or of mice treated with certain steroids, e.g., progesterone, testosterone (Robson and Sharaf<sup>3</sup>). The effect of pregnatrienone on this response was investigated. Mice were ovariectomised and injected with 1 mg., or 5 mg. of pregnatrienone in oil daily for 6 days and the uterus tested *in vitro* on the following day. Sodium œstrone sulphate produced contraction of the uterus of mice treated with 1 mg. per day, but inhibition of those receiving 5 mg. per day. In this respect, therefore, pregnatrienone has about 1/5 the activity of progesterone.

*Androgenic effects.* Mature rats were castrated and left for 3 months. Groups of 5 were then injected with 1 mg. and 3 mg. of pregnatrienone in oil daily for 10 days, i.e., the total dose per rat was respectively 10 mg. and 30 mg. Control groups were injected with oil. On the day after the last injection the animals were killed and the seminal vesicles and prostates weighed. There was no significant difference between control and treated groups. Hence pregnatrienone produced no measurable androgenic effect.

We are greatly indebted to Dr. J. K. Norymberski of the British Schering Research Institute for the pregnatrienone used, and to the Medical Research Council for a grant (to J.M.R.) which defrayed part of the expenses of this investigation.

### REFERENCES

1. Höhn and Robson, *J. Physiol.*, 1950, **3**, 174.
2. Robson, *J. Physiol.*, 1938, **92**, 371.
3. Robson and Sharaf, *J. Endocrinology*, 1950 (in the press).