

clusion that they were not spectroscopically identical. Furthermore, comparison between normal serum containing traces of hemato-porphyrin and pellagrous serum left no room for doubt that this substance, at least in any detectable quantity, is not present in the circulating blood of pellagra victims.

Three and one half liters of urine from an acute case were concentrated *in vacuo*, extracted with alcohol, the residue from the alcohol evaporation taken up with acid, and the examination carried out in the usual manner. The spectrogram showed no evidence of the presence of hematoporphyrin.

4589

### A Crystalline Substance of the Hypophysis Which Promotes Follicular Growth.

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While working with an acid alcohol extract of the anterior lobe of the pituitary body, according to the earlier method of Hisaw, Fevold, and Meyer,<sup>1</sup> it was found possible to produce 2 very different ovarian reactions depending upon the dosage used. When a *small* amount of the extract was injected into adult rats, follicular growth increased and the rats remained in a condition of oestrus much longer than normally. On the other hand, if a *larger* amount of the same extract was injected the follicles in the ovary became atretic with the formation of corpora lutea without ovulation, the animal remaining in a state of dioestrus.

Attempts were then made to separate the extract into fractions which would give one of the above mentioned physiological effects without the other. This was done by following the unpublished technique used by Hisaw in making an extract of corpus luteum hormone. An acid alcohol extraction of desiccated anterior lobe was, during the process of purification, separated into one fraction which was soluble in absolute alcohol and one which was not. From the latter a crystalline product was secured which induces precocious sexual maturity. Such crystals when injected in aqueous solution into 18 day old mice, in amount equivalent to  $\frac{1}{2}$  gm. of fresh material per day, invariably caused the vagina to open in from 2 to 3

<sup>1</sup> Hisaw, F. L., Fevold, H. L., and Meyer, R. K., *Phy. Zool.*, 1929, in press.

days. Normally the vagina remains closed until about the thirty-fifth day (30th to 49th day). The ovaries of the treated mice showed numerous and large mature follicles and in those animals which were not killed ovulation always occurred.

However, when an equal, daily amount of the fraction soluble in absolute alcohol was injected into similarly immature mice, the vagina did not open until the animals were from 31 to 37 days old, which is about the normal age of sexual maturity. The large follicles of such individuals became filled with lutein tissue, the ova within disintegrated, and no ovulation took place. A cross section of the ovary of such an animal looks much like that described by Aschheim and Zondek<sup>2</sup> in mice injected with urine from pregnant women, while the cross section of an ovary of a mouse injected with the crystalline fraction resembles that found by Smith and Engle,<sup>3</sup> after daily transplant of the anterior lobe. It may be that the secret of the apparent divergence in the results of these respective investigators lies in the existence of 2 different substances as indicated by the fractions just described.

By administering daily transplants of the anterior lobe of the pituitary, Smith and Engle, for instance, induced precocious maturity in female mice and rats with increased follicular growth and subsequent ovulation. Aschheim and Zondek, on the contrary, working with urine of pregnant women, which is supposed to contain anterior lobe hormone, found quite a different picture in the ovaries of injected mice. The large, abundant follicles became hemorrhagic, forming what they termed "blutpunkte". Luteinization of the follicle and degeneration of the ovum occurred producing corpora lutea without ovulation. This, Aschheim and Zondek attributed to the anterior pituitary hormone in the urine.

Evans and Simpson<sup>4</sup> recently recognized 2 hormones in the anterior lobe: one a maturity producing substance, which was found in acid aqueous extract of the anterior hypophysis, in the placenta, and in urine from pregnant women, the other obtained in alkaline aqueous extract, a growth producing hormone which at the same time caused luteinization of the follicles and inhibition of ovulation. The former seems to agree more closely with the crystalline fraction previously mentioned. Other experiments are being carried on at the present time to test further physiological effects of the substances described in this paper.

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<sup>2</sup> Aschheim, S., and Zondek, B., *Klin. Wchnschr.*, 1928, vii, 1404.

<sup>3</sup> Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1928, xl, 159.

<sup>4</sup> Evans, H. M., and Simpson, M. E., *J. Am. Med. Assn.*, 1928, xc, Nr. 18.