

was fed as the nitrate in amounts of 0.5 mg. of metal per rat per day; copper, cobalt and manganese as the chlorides in amounts of 0.1 mg. of metal per rat per day.

Hemoglobin determinations were made by the method of Newcomer.

The results of the experiments are briefly summarized in Table I.

It is evident, therefore, that under the conditions of our experiments *pure* iron, fed alone, does not cause a regeneration of hemoglobin in anaemic white rats. Copper is effective in the regeneration when fed together with iron, while manganese and cobalt fed under the same conditions are without effect.

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Effect of Placental Extracts on Ovarian Stimulating Properties of Anterior Hypophysis.*

JOHN C. BURCH AND R. S. CUNNINGHAM.

From the Department of Gynecology and Anatomy, Vanderbilt University School of Medicine, Nashville, Tennessee.

The interrelationships between the hypophysis and the ovary have been studied extensively. Changes in the ovary following the administration of anterior lobe substance and extracts have been described by Goetsch,¹ Evans,² Zondex and Ascheim,³ and others. Erdheim and Stumme⁴ called attention to changes in the hypophysis during pregnancy. Zondex and Ascheim have demonstrated, in the urine of pregnant women, the presence of a hormone which has all the ovarian growth properties of the anterior hypophysis, and have utilized this in their test for pregnancy. Fels⁵ found the same hormone in the blood of pregnant women. Recently Engle and Smith⁶ have demonstrated that the amount of ovarian stimulating substance in the hypophysis of the guinea pig varied during the sexual cycle, and was much diminished during the time the vagina

* Part of the animals used in these experiments were drawn from the colony supported by the Commonwealth Fund.

¹ Goetsch, Emil, *Johns Hopkins Hosp. Bull.*, 1916, xxvii, 29.

² Evans, Herbert M., *Harvey Lectures*, 1924, xix, 212.

³ Zondex, B., and Ascheim, S., *Arch. f. Gyn.*, 1927, cxxx, 1.

⁴ Erdheim, J., and Stumme, E., *Beitg. z. Path. Anat. u. z. Allg. Path.*, 1909, xli, 1.

⁵ Fels, Erich, *Wien. Klin. Woch.*, 1928, xli, 1225.

⁶ Smith, P. E., and Engle, E. T., *Anat. Rec.*, 1929, xliii, 239.

was open. Evans and Simpson⁷ further showed that this substance was increased by castration, and was present in larger amounts in males than in females.

From the foregoing work the following facts are known: (1) the hypophysis has a powerful action on the ovary; (2) the ovary affects the hypophysis; (3) there is a change in the hypophysis during pregnancy. With these conclusions in view, it seemed reasonable to believe that the ovarian growth stimulating properties of the anterior hypophysis could be increased by the injections of placental extracts which contain a high concentration of oestrin.

Our experiments tend to support this belief. Adult female rats, of approximately the same weight, were castrated, in order to exclude any cyclical variation, allowed to recover for 2 weeks, and then given a series of injections of a commercial alcoholic extract of human placenta which had been carefully standardized. The injections were given for 6 days and varied from 5 to 25 rat units. The animals were sacrificed and the anterior lobe of the hypophysis implanted into infantile mice of 8-12 gm. weight. (In none of these was the vaginal orifice open at the beginning of the experiment.) Control mice were implanted with hypophyses from castrated rats which had not been injected with the extract. Each mouse received 2 hypophyses which were implanted on successive days, and the mice were sacrificed on the fourth day of the experiment.

Our series of experimental mice included 32 animals, and there were 16 controls (*i. e.*, mice receiving hypophyses from rats which had been castrated but had not received placental extract.) The most noteworthy gross difference was the uniformly larger size of the ovaries in the experimental animals, the average difference being approximately in the ratio of 5 to 2. In addition, in the experimental animals, the bursae were enormously distended with fluid which often contained blood. In both series there were many ripe follicles and maturing corpora lutea; these were more numerous in the experimental animals and often contained blood. From 6 to 8 hemorrhagic follicles were found in the ovaries of the experimental animals, whereas only 2 to 3 at most were seen in the controls. Thus, while the changes in the experimental series were in general similar to those in the controls, they were markedly exaggerated.

⁷ Evans, Herbert M., and Simpson, Miriam E., *Anat. Rec.*, 1927, xxxv, 36.