

by Nicholls and Perlzweig⁶ and for which they reported decreased total and unchanged unsaturated fats. This militates against the conclusion of Jobling and Peterson⁷ that the antitryptic substances of the blood serum are identified in the unsaturated fatty acids.

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Impairment of the Birth Mechanism Due to Hormones from the Anterior Hypophysis.*

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It has been shown in this laboratory¹ that the administration of the hypophyseal growth hormone (alkaline extracts of bovine hypophysis) during the last week of pregnancy in some way injures the birth mechanism. Treatment is stopped on day 21. There is then a characteristic prolongation of pregnancy of from 2 to 3 days, with final birth of dead or living foetuses. There are also instances of complete failure even to give birth to dead foetuses and of the consequent resorption of the latter. The effect has been shown to be due in all probability to changes which the treatment provokes in the ovaries of the pregnant animal, more especially to the formation of fresh lutein tissue there.²

Now another hormone of the anterior hypophysis, one of the outstanding characteristics of which is the production of precocious maturity in young female rodents, strangely enough, in addition to its marked stimulation of the follicular apparatus also causes the luteinization of follicle walls, a point strongly emphasized by Zondek and Aschheim.³ It might be expected, therefore, that whatever effects from growth hormone treatment are due to the creation of fresh lutein tissue in the ovary would also be encountered in the treatment of animals with this second hormone from the anterior hypophysis.

We propose to show that this is the case as regards interference

⁶ Nicholls, E. G., and Perlzweig, W. A., *J. Clin. Inv.*, 1928, v, 181.

⁷ Jobling, J. W., and Peterson, W., *J. Exp. Med.*, 1914, xix, 459.

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¹ Teel, H. M., *Am. J. Physiol.*, 1926, lxxix, 170.

² Dispensa, J. G., M.A. Thesis, University of California, May, 1928 (unpublished).

³ Zondek, B., and Aschheim, S., *Deutsche med. Wochschr.*, Feb. 19, 1926; *Ztschr. f. Geburts. u. Gynäk.*, 1926, xc, 372, 387.

with the mechanism of birth. Engle⁴ has recently doubted the existence of these effects. His method consisted in daily implantation into the pregnant animal of anterior hypophyseal tissue—the most effective method, it must be admitted, of provoking the precocious maturity of young female rats and mice. The characteristic prolongation of gestation can be secured by anterior hypophyseal implants, for instance, by 1 or 2 glands daily for the last 5 days of gestation. By administering a single hypophyseal implant from a gonadectomized male every other day beginning on day 12 of gestation, the birth mechanism was destroyed in 8 of 10 cases. Extracts of the ripe human placenta and of the urine of pregnant women[†] gave us the opportunity for another type of dosage with this hormone. For many months we have had such extracts in hand, solutions proven to contain neither folliculin nor the growth hormone.[‡] With these we have secured the same interference with the birth mechanism in pregnant rats so characteristic of treatment with the growth hormone.

We would emphasize the fact that, unlike the invariable effect of the growth hormone, the administration of the maturity hormone does not hurt the birth mechanism in all cases. In the case in which the maturity hormone was administered by the implant method and hence greatly stimulated the follicular apparatus, folliculin was, of

⁴ Engle, E. T., and Mermod, C., *Anat. Record*, 1928, xxxviii, 11.

[†] Our extracts from the urine of pregnant women are prepared by methods which we find resemble closely those just published by Biedl (*Endokrinologie*, 1928, ii). The urine is slightly acidified (green-blue to Brom Thymol Blue), filtered and concentrated to 1/8 volume in vacuo (35° C.) and filtered; ethyl alcohol is added to 75%. The mixture is centrifuged and the residue dissolved in water. The precipitation from 75% alcohol is repeated twice. The solid matter left after the third alcohol precipitation is dissolved in water, centrifuged, and the supernatant fluid dialyzed 16 hours. (Sometimes the extract has been evaporated to dryness and extracted twice with ether, then redissolved in water. This step was inserted to make doubly sure of the absence of folliculin.) The extract obtained is colorless and clear, gives no biuret reaction, has total solids of 0.2 gm per 100 cc. and when injected intramuscularly or subcutaneously is able to mature 24 day old rats in 1/16 cc. daily dose for 3 days. The placenta extracts though less pure have been equally potent (3/16 cc. total dose). They have been prepared by extracting fresh (or frozen) human placenta with weak acid (500 gm. ground placenta + 800 cc. water + 160 cc. 0.2/N acetic acid). Folliculin was removed by extraction with ether.

[‡] A total of 9 cc., for instance, (distributed in 9 doses) has been injected subcutaneously in spayed females over a period of 2 days without provoking oestrous smear changes. The same solution provoked the maturity of 24 day old rats within 4 days when given in 3 daily doses of 1/16 cc. each. Nor was there evidence that the solution contained the growth hormone, as tested by its administration in 2 cc. daily quantities intraperitoneally to 5 months old normal females.

course, produced in considerable quantity in the affected gonad. It is to the coincident presence of this hormone that we would attribute the normality of the birth mechanism which we have encountered in high dosage with the implant method (8 rat glands per day). It does, in fact, occasionally bring about premature birth through a folliculin effect. On the other hand, the administration only once daily of a highly concentrated fraction out of human placenta or urine of pregnant women has given the characteristic birth retarding effect.

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Stimulation of Placentoma Reaction in Virginal Endometrium by Treatment with Anterior Hypophyseal Hormone.

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It has been shown that the anterior hypophyseal growth hormone markedly aids the placentoma reaction of the endometrium of adult virginal rats, tumors of this sort being provoked about silk threads when simultaneous dosage with the growth hormone is carried out.* The anterior hypophyseal hormone which promotes precocious development of the immature ovary, has a similar effect if it is not administered so as to stimulate greatly the follicular apparatus and lead to the formation of much folliculin. It is for this reason, we believe, that the administration of forms of the hormone (extracts of the urine of pregnant women and of human placenta) are more efficacious in stimulating placentomata than is the implant method.

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Hyperplasia of Mammary Apparatus in Precocious Maturity Induced by Anterior Hypophyseal Hormone.

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Within 6 days, the mammary tree of 24 day old female rats is clearly increased in complexity by all methods of administration of

* Whatever the substance injected, it is a routine to give 3 days preliminary treatment and 5 days treatment after insertion of the threads, autopsy occurring on the sixth day after the threads were inserted.