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Excessive Anterior-Pituitary-Like Hormone and Variations in Oestrin in the Toxemias of Late Pregnancy.

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(Introduced by Harvey Cushing.)

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Quantitative determinations of the anterior-pituitary-like gonad-stimulating hormone and of oestrin have been made on the sera and urines of 27 women, both normal and toxemic, during late pregnancy, *i. e.*, from 7½ months to term. The Ascheim-Zondek and Allen-Doisy methods have been employed. Ten cases were normal, 14 were diagnosed toxemia without convulsions and 3 had eclampsia.

The following procedure was carried out in every instance. A mixed 24-hour specimen of urine was collected and measured. Forty cc. of blood were allowed to clot and the serum separated. For the Ascheim-Zondek test the amounts of urine and sera to be assayed were precipitated with 5 volumes of 95% alcohol, allowed to stand overnight and centrifuged. The precipitate was washed with ether and taken up in saline for injection into female rats 3 weeks old. A test was considered positive only if corpora lutea were grossly visible. In establishing the hormone content of each urine and serum 5 to 20 rats were used, depending upon how well the results agreed. For the Allen-Doisy assay extracts of the serum were made by precipitating the proteins with 95% alcohol, extracting the precipitate repeatedly with alcohol and ether, evaporating the combined supernatant fluids and taking up the residue in saline for injection into mature spayed female rats. The urine was not extracted. Six to 24 rats were used for establishing the oestrin content of each specimen, the smaller number being often necessary in the assays on sera because of the limited amount of material. The rats used were frequently tested with oestrin of known potency. A full oestrous smear in half the rats into whom a given amount of specimen was injected was considered positive.

In both Ascheim-Zondek and Allen-Doisy determinations the amount of hormone in the 24-hour volume of urine was calculated on the basis of the smallest quantity that would give a positive test. The use of 24-hour volumes of urine deserves especial emphasis because of the obvious fallacy of attempting to compare results of

* The Mrs. William Lowell Putnam investigation of the toxemias of pregnancy.

any quantitative urine determinations without some gauge of the concentration of the specimens analyzed.

In the Ascheim-Zondek tests on 10 normally pregnant women, all but 2 of whom were 3 weeks or less from term, as much as 1.5 cc. to 2.5 cc. of serum was required to give a positive result, the average figure being 2.05 cc. The urinary excretion varied from 325 to 900 r.u. in 24 hours, the average figure being 540 r.u.

In the Ascheim-Zondek tests on 14 patients diagnosed as toxemic without convulsions, all but 3 of whom were 3 weeks or less from term, the smallest amounts of sera that would give positive results lay between 0.07 cc. and 1.0 cc., the average figure being 0.51 cc. The urinary excretion varied from 1230 to 13000 r.u. in 24 hours, the average figure being 4216 r.u.

It was impossible to collect 24-hour urines on the 3 eclamptic patients. Two of them were positive for the gonadotropic hormone with as little as 0.2 cc. of serum and the third was positive with 0.025 cc.

The 10 normally pregnant women showed excretion of oestrin varying between 4200 and 7500 r.u. in 24 hours, the average being 6000 r.u. In every instance 3 cc. of the sera of these women gave full oestrous smears, and in all but 2 of them 2 cc. stimulated full oestrous.

There were strikingly wide variations in the urinary excretion of oestrin by the 14 patients diagnosed as toxemic without convulsions, the figures lying between 310 and 10,000 r.u. in 24 hours, with an average of 3800 r.u. The excretion of only 4 of these patients lay within normal limits. Nine of the remaining 10 excreted less than the normal amount. Of their sera, 9 were completely negative and 5 were positive for oestrin in 3 cc. amounts. Three of these 5 were completely negative in 2 cc. amounts.

Of the 3 eclamptic sera, one gave a positive Allen-Doisy test with 2 cc., one gave a positive test with 3 cc., but negative with 2 cc., and the third gave a negative with 3 cc.

It would appear, therefore, that the blood and urine of toxemic patients in late pregnancy contain excessive amounts of the anterior-pituitary-like hormone, and wide variations in oestrin with a decided tendency toward low levels. Preliminary experiments with hypophysectomized rats indicate that the excessive gonadotropic hormone of these toxemias may be hypophyseal in origin.