

with a specific associated substance which takes place as soon as the latter has been made accessible to the salt.

Furthermore, it seems that we can distinguish at least 3 different effects of salts in their interaction with the urease: (1) Specific combinations of kations with the enzyme or with associated substances. In these combinations alkali earths are by far the most favorable. (2) Injurious salt effects of a non-specific character. Salts of heavy metals are more injurious than salts of alkali earths and the latter are more injurious than salts of alkali metals. (3) In addition osmotic effects of salts play in all probability a certain rôle. Increased osmotic pressure of salts or of non-electrolyses, at least within the range we have examined so far, acts favorably on the enzyme. Furthermore, we have found specific actions of proteins which may modify the effect of salts on urease.

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<sup>1</sup> Loeb, Leo, and Bodansky, O., *J. Biol. Chem.*, 1927, lxxii, 415.

3839

### Sex Characteristics in Monkeys.

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Female monkeys during sexually mature life show the sex characteristics of reddening and swelling of the skin about the external genital organs, on the buttocks and medial surfaces of the thighs. These phenomena disappear after double ovariectomy and can again be induced in spayed animals by injections of ovarian and placental extracts.<sup>1</sup> Three male monkeys in our colony had never shown this cutaneous reddening. (It has, however, been reported that male monkeys may show this reddening during the breeding season.) During the late summer and fall the 'sexual skin' of a large 7-year-old male began to redden. During November and December the regions affected covered an area 15x13 cm. in extent. The reddening reached a moderate intensity but never approached the maximum 'sexual skin' color of the mature female. From our experiments with ovarian hormone in inducing this condition in spayed animals, it seemed logical to infer that this condition in the male might be due to the male sex hormone.

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Needels<sup>2</sup> had previously reported a series of blood tests in our monkeys by a modified Manoilov technique, a test supposed to distinguish male from female blood. To our great surprise the blood of this fully grown, finely developed, 6-year-old male had consistently given a 'female' reaction. Two younger males, one of which was immature, returned typical 'male' tests. This test seemed essentially a reduction reaction, the male blood usually causing a greater reduction of the reagents than the female blood. But Needel's results indicated fluctuation especially in females when tests were repeated upon the same individuals. Consequently a graded series of color standards were prepared for comparison. The tests ranged from no decolorization ('female') to complete decolorization ('male').

Several conclusions were drawn: (1) There was a distinct variation in individual female monkeys during the menstrual cycle. At or near menstruation the tests showed less decolorization, while during the intermenstrum greater decolorization (an approach toward the 'male' reaction) occurred. The intermenstrum is the time when follicles are largest and secondary sex phenomena most marked—the time when the ovaries are supposedly most actively secreting hormone.<sup>1, 3</sup> Consequently, if this reaction were specific for sex, the opposite variation, toward the other ('female') end of the scale, would be expected. (2) After ovariectomy less decolorization of reagents occurred. (3) When ovarian and placental extracts in oil were injected into the ovariectomized animals there was a greater decolorization—a shift toward the 'male' end of the scale.

Needels agreed with Riddle and Reinhart<sup>4</sup> in the opinion that this test, instead of being specific for sex, was really dependent upon metabolic level. In a majority of cases, however, the Manoilov reaction did place the individual as to sex.

Since the skin reactions under consideration are similar, the blood reaction (Manoilov) of the normal female when ova are ripening approaches the 'male' reaction and the particular male described had consistently given a 'female' reaction, one might infer a similarity in male and female sex hormones. Such a similarity has been reported by Fellner,<sup>5</sup> Robinson and Zondek,<sup>6</sup> and Laquer.<sup>7</sup> They find that extracts of testis injected into female test animals may give results somewhat similar to ovarian extracts. Doisy, Ralls, Allen and Johnston<sup>8</sup> reported negative results in attempts to induce oestrus in spayed rats from injections of lipoid extract of beef testicle.

The success of Smith and Engle<sup>9</sup> and of Zondek and Aschheim<sup>10</sup> in the use of 'implantation' of fresh tissues for the demonstration of

hormone effects and the limited amount of testicular tissue available suggested the use of fresh material. Consequently, on December 13th the left testis was removed from this monkey. It measured 49.5x36x34 mm. and weighed (without the epididymis) 31.38 gm. The weight of the epididymis alone was 4.42 gm. Comparison of the weight of this testis with the average cited for the human testis (10.5 to 14 gm.<sup>11</sup>) shows it to be more than twice the average for man, in spite of the fact that this full grown monkey weighed less than 30 pounds. Sperm from the epididymis and proximal portion of the *vas deferens* were extremely motile. The testis and epididymis were cut up separately, ground up in a small amount of Ringer's solution and injected subcutaneously into a series of 10 ovariectomized rats. Four rats received five 1 cc. doses spaced over 26½ hours, 3 rats received 4 injections, and 3 rats received 3 injections during shorter periods. The dosage of testis substance received by the rats ranged from 1/12 to 1/20 of the total testis. The dosage of epididymis substance ranged from 1/4 to 1/7 of the total. The Ringer suspension was kept on ice in a rubber stoppered sterile bottle during the interval to minimize deterioration. In none of the 10 rats injected was there the slightest indication of even a partial oestrous reaction as determined by the vaginal smear method.

These results, therefore, offer no positive evidence for a similarity of action of testicular hormone to that of ovarian hormone in producing substitution effects in spayed females. They do not, however, rule out the possibility that highly concentrated extracts might do so.

From Needels' results with the Manoilov test it would seem that both male and female hormones act in a similar way (but in different degrees) upon the reduction factor of the blood. Surely the 'sexual skin' characteristics of the large male described were very similar to such conditions in the female.

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<sup>1</sup> Allen, E., Carnegie Inst., Washington, 1927, Pub. No. 380, 1.

<sup>2</sup> Needels, L. J., *Anat. Rec.*, 1927, xxxii, 238.

<sup>3</sup> Corner, G. W., Carnegie Inst., Washington, 1923, Pub. No. 332, 73.

<sup>4</sup> Riddle, O., and Reinhart, W. H., *PROC. SOC. EXP. BIOL. AND MED.*, 1927, xxiv, 359.

<sup>5</sup> Fellner, O. O., *Pflüger's Arch.*, 1921, clxxxix, 199.

<sup>6</sup> Robinson, M. R., and Zondek, B., *Am. J. Obst. and Gyn.*, 1924, vii, 83.

<sup>7</sup> Laquer, E., *Klin. Wochenschr.*, 1927, vi, 390.

<sup>8</sup> Doisy, E. A., Ralls, J. O., Allen, E., and Johnston, C. G., *J. Biol. Chem.*, 1924, lxi, 711.

<sup>9</sup> Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1927, xl, 159.

<sup>10</sup> Zondek, B., and Aschheim, S., *Klin. Wochenschr.*, 1927, vi, 248.

<sup>11</sup> Gray's Anatomy.