

not protect the guinea pigs from the demineralizing effects of experimental hyperparathyroidism. It is possible, however, that the healing of bone lesions in experimental or clinical hyperparathyroidism would still be promoted by viosterol after the state of hyperparathyroidism had been terminated by discontinuance of parathormone administration in experimental animals, or by the removal of a parathyroid adenoma in clinical cases.

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**Effects of Hypophyseal Extracts on Sexually Immature Monkeys.\***

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Information concerning the effects of anterior pituitary materials on the gonads of primates is very limited. E. Allen<sup>1</sup> and Hartman<sup>2</sup> have demonstrated the gonad stimulating effect of hypophyseal implants using dogs, monkeys, and pigs as donors, and Courier, *et al.*,<sup>3</sup> have shown that similar effects can be obtained with alkaline hypophyseal extracts. We wish to report the results of injecting aqueous pyridine extracts of anterior pituitary material in immature female *Macacus rhesus* monkeys.†

Aqueous pyridine extracts as prepared by Fevold, *et al.*,<sup>4</sup> were used. The preparations were injected subcutaneously in 0.5 cc. doses twice daily for periods of 14 to 16 days and each cc. of extract was equivalent to 1 gm. of dried pituitary powder. As small a dose as 8 gm. equivalent of pituitary was found to be sufficient in one animal. The first noticeable change observed was the appearance, in 2 to 3 days of injection period, of a purplish coloration in the skin of the peri-anal region and a reddening of the nipples of the mammae. The maximum coloration and peri-anal swelling was reached in about 8-12 days, the vaginal smear at this time showing predominantly cornified cells. When the injections are

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\* Aided in part by grants from the National Research Council, Committee on Problems of Sex.

<sup>1</sup> Allen, E., *Anat. Rec.*, 1928, **89**, 315.

<sup>2</sup> Hartman, C., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **27**, 338.

<sup>3</sup> Courier, R., Kehl, R., Raynaud, R., *C. R. S. de Biol.*, 1929, **101**, 1093.

† The pituitary powder was kindly furnished by the Research Laboratories of Parke, Davis and Company.

<sup>4</sup> Fevold, H. L., Hisaw, F. L., Leonard, S. L., *Am. J. Physiol.*, 1931, **97**, 291.

continued further the coloration decreases somewhat but the oedematous condition in the inguinal region and the posterior part of the thigh becomes progressively greater. No blood could be detected in the vagina although uterine bleeding (follicular menstruation) followed the cessation of injections.

The effects of the treatment on the internal sexual organs were very marked. The ovaries increased in weight as much as 1800%, the increase being due to development of a number of large follicles. Corpora lutea were entirely absent except in one doubtful case where there seemed to be slight luteinization. Pyridine extracts, which produced both follicular and corpus luteum development in rats, stimulated only follicular development in monkeys, and these ovaries could not be luteinized when such treatment was followed by intraperitoneal injections of strong luteinizing fractions but instead the ovaries retrogressed to the immature state during which menstruation occurred. The uterine endometrium in no case showed corpus luteum effects but was of the type characteristic of follicular activity which can be duplicated in castrates by administering follicular hormone. If these animals are castrated after anterior lobe treatment and given corpus luteum hormone (corporin) an endometrium of the corpus luteum type is developed.

No instances of ovulation were observed nor could it be induced in the stimulated ovaries by intravenous injections of from 400 to 800 times the amount of anterior lobe extract necessary to elicit ovulation in rabbits.

When immature monkeys were given pituitary extracts, as described above, there was a marked growth of the mammary glands but lactation did not occur during or after cessation of treatment. In those cases, however, where anterior lobe treatment was followed by castration and injections of corpus luteum extracts lactation was quite pronounced.

Dried pyridine extracts put up in gelatin capsules and inserted into the vagina of an immature monkey in daily doses equivalent to 1 gm. of dried pituitary powder, for 9 days produced no noticeable vaginal or sexual skin changes.

Monkeys weighing 3000 to 3500 gm. apparently respond more readily and give a more exaggerated picture than those weighing about 1800 gm. This is presumably due to a difference in age though all animals used were sexually immature.

It seems, from these results, that monkeys may differ from laboratory rodents in their response to anterior lobe extracts with regard to development of lutein tissue and perhaps ovulation, otherwise

they give the same fundamental reactions known for other mammals. Yet these differences may be only apparent and due to some factor not controlled in the experiments.

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### New Studies on the Filtrability of the Tubercle Group.

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A grass bacillus indistinguishable in the characteristic cultural and morphological earmarks from the tubercle bacillus was isolated 6 years ago. Its acid fastness was variable even in cultures isolated from a single cell. Under certain conditions it developed non-acid-fast granules which were filtered through a Berkefeld N candle. These underwent slow and capricious germination to a non-acid-fast, diphtheroidal bacillus whose cultural characters were quite different from the antecedent strain. Microscopically, however, the strains were almost indistinguishable.

In 4 out of 6 years of the intervening period, and always in the spring of the year, the identical diphtheroid has spontaneously dissociated from the original strain, indicating that the mechanism for such dissociation is *via* the filtrable gonidial granule. (Much.)

More recently, by employing a modified K-medium (Kendall) these observations have been repeated and extended; for in addition to the diphtheroidal form, the original cultural stage of the organism has been recovered from the filtrates. A strain of bovine tubercle bacillus has also dissociated a very similar diphtheroidal strain, often containing numerous acid-fast granules.

These strains differ in no essential particular from the diphtheroids of Hodgkin's disease, benign lymphogranulomatosis and Boeck's sarcoid, making it highly probable that their origin *in vivo* is also the tubercle bacillus. No opinion is vouchsafed in respect of their rôle in the pathogenesis of such diseases.

For almost 30 years non-acid-fast forms have been described for tubercle bacillus by various workers, but their mechanism of origin has never been clear and the strains themselves were viewed as contaminants.

This final demonstration that single-celled cultures of the acid-