

basement rocks comprising the Coahuila Peninsula have been brought together; their lithology and structure have been summarized; the size and position of the peninsula have been revised; the probable source of much of the coarse agglomeratic material in the neritic facies of the Neocomian and Upper Jurassic of northern Mexico has been found in the basement rocks of the Coahuila Peninsula.

XI. The similarity of certain faunal elements in the Upper Jurassic and Neocomian sediments of California and Northern Mexico suggests that seas which occupied these geosynclines were at times connected across northern Mexico. The scattered faunal evidence bearing on this paleographic problem has been assembled.

LEWIS B. KELLUM

UNIVERSITY OF MICHIGAN

## SPECIAL ARTICLES

### THE BIOLOGIC EFFECTS OF PINEAL EXTRACT (HANSON)<sup>1</sup>

IN a previous communication on September 21, 1934, attention was called to the biological effects of thymus extract (Hanson) on accruing acceleration in growth and development in each successive generation of young born to succeeding generations of parents under treatment. At that time it was stated that similar studies had been undertaken with other hormones and glandular products. The results to date with pineal extract (Hanson) are, in our opinion, of such interest as to warrant publication.

The extract employed most frequently (PB<sub>22</sub>) was one of several prepared by Hanson. It represents an aqueous acid derivative, probably in the form of a picrate, and containing 0.21 per cent. free picric acid. It is relatively non-toxic but somewhat irritating locally. One can not, however, escape the impression that it is somewhat of a deterrent to the general good health of the rats in the experiments herein described. To date more refined extracts seem to lack the activity apparent in PB<sub>22</sub>. Further studies in this field are in progress.

To date five successive generations of the pineal strain of rats have been under observation. An analysis of the biological data of each of these generations reveals significant facts. In the first generation no effect is apparent other than moderate loss of weight and phenomena suggestive of sex excitation and early breeding. In the second generation there is definite retardation in growth, with mild precocity in gonadal development. In subsequent generations, the third to the fifth, there is accruing retardation in growth with accruing acceleration in gonadal and bodily development. Precocious "dwarfism" with relative macrogenitalism are the outstanding result. In addition eye anomalies, ocular diseases and blindness are extremely common.

<sup>1</sup> From the Philadelphia Institute for Medical Research, from the Samuel Bell, Jr., Laboratory in the Philadelphia General Hospital, the Laboratories of the Philadelphia General Hospital, Philadelphia, Pennsylvania, and the Hanson Research Laboratory, Faribault, Minnesota. We wish to acknowledge with gratitude the financial assistance given one of us, Dr. Hanson, by the Josiah Macy, Jr., Foundation.

The effects of pineal extract on growth is revealed in Fig. 1, which represents the growth curve of the

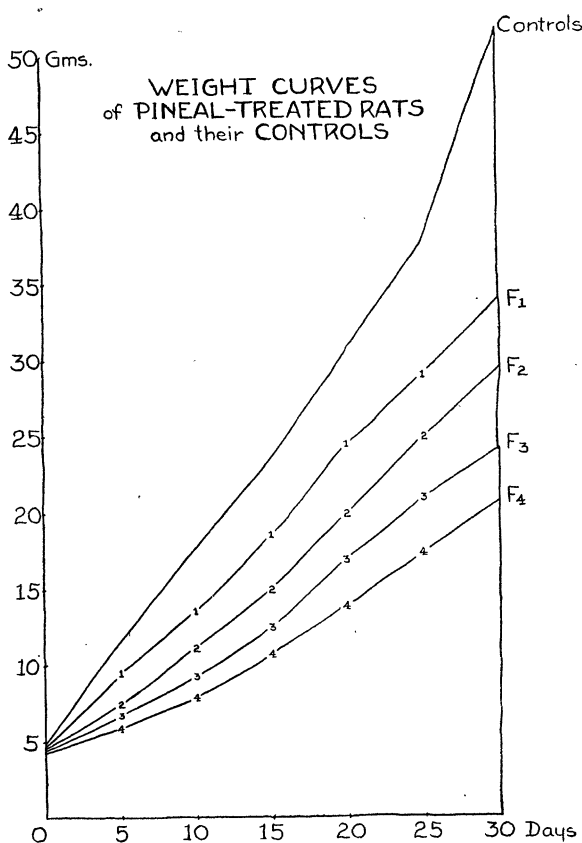


FIG. 1

young of five successive generations of rats treated with pineal extract. The "dwarfism" resulting from pineal extract (Hanson) is usually permanent, though less striking as the animals age. In rats of the second or later generations, perhaps less than 10 per cent. attained normal weight or growth. The early employment of potent extract in the young almost always insures more striking and more permanent "dwarfism."

Though small in size, the resulting animals are precocious in development. The acceleration in differentiation is shown in Table 1. Lack of uniformity in

PROGRESSIVE DEVELOPMENT UNDER PINEAL TREATMENT

	Ears Opd.	Teeth Erupt.	Fur Appd.	Eyes Opd.	Testes Descd.	Vagina Opd.
Controls	2½-3½ (3)	8-10 (9.0)	16 (16)	14-17 (15.5)	31-40 (38)	55-72 (65)
F <sub>1</sub>	2-3 (3.3)	8-10 (9.0)	7-16 (13.0)	12-17 (14.9)	12-36 (22.0)	32-56 (45.0)
F <sub>2</sub>	2-3 (2.8)	7-11 (9.0)	6-17 (12.0)	12-16 (13.8)	6-26 (15.0)	30-39 (37.0)
F <sub>3</sub>	2-3 (2.3)	5-8 (6.9)	5-12 (9.0)	5-13 (9.8)	5-12 (10.0)	29-39 (32.0)
F <sub>4</sub>	1-3 (2.0)	3-5 (4.0)	4-8 (5.0)	4-8 (6.0)	4-9 (5.0)	23-26 (24.0)

The number of rats constituting the basis for the weight curves is as follows: For the controls, 301 rats, for the F<sub>1</sub> Generation, 138 rats, for the F<sub>2</sub> Generation 543 rats, for the F<sub>3</sub> Generation 155 rats and for the F<sub>4</sub> Generation 41 rats.

size and in the rate of growth and development of individual members of a litter is striking. Because of this variability, the range of values, as well as the average, is presented in the accompanying table.

The compiled data on both the growth and development, as expressed in tables and curves, reveal the same step-like progression in succeeding generations under treatment as was evidenced in our thymus-treated strain of rats. However, in the pineal studies there appears a paradox, a dissociation of the effects on growth and differentiation. The progressive accruing effect is in two or possibly three directions, retardation in growth accompanied by acceleration in gonadal development and also in bodily differentiation.

Caution must be exercised in interpreting these biological effects as indicating the functions of the pineal gland. If such were the case, then one should expect pinealectomy to result in enhanced growth and retarded development. Such, however, is not the case to date in the majority of instances in a small series of rats subjected to pinealectomy in our institute by Dr. N. H. Einhorn. Further studies in this connection are desirable.

From the foregoing it is evident that our results in the study of many hundreds of rats do not conform entirely to any of those reported in the literature. It is true that in common with the majority of workers we have observed little of significance in the first generation under treatment. In the subsequent generations we have found consistently "dwarfism," rather than overgrowth. Precocity, however, has been observed in all our animals from the third generation on and this concerns both gonadal and bodily development. The resulting animal is small, usually half or less than half the normal size, during the early weeks of life, precocious in development, with gonads suggesting the macrogenitalism seen clinically in certain types of tumor of the pineal gland. In addition the animals are physically weak and appear more irritable and nervous than normal, and eye anomalies abound.

## CONCLUSIONS

Pineal extract (Hanson) has retarded the rate of growth and accelerated the rate of differentiation and has hastened the onset of adolescence in the offspring of treated parents. The end result is "dwarfism" with precocious development and relative macrogenitalism.

The injection of succeeding generations of parent rats has resulted in the amplification of these biologic effects in succeeding generations of their young.

L. G. ROWNTREE

J. H. CLARK

ARTHUR STEINBERG

A. M. HANSON

## ARTIFICIAL CONTROL OF NUCELLAR EMBRYONY IN CITRUS

THE supernumerary embryos, other than those of seminal origin, which develop from seeds of most species of citrus and related genera were identified as cases of nucellar embryony by Strasburger,<sup>1</sup> a form of sporophytic budding.<sup>2</sup> It has been repeatedly noted that the number of embryos developed from individual seeds may vary from one to many in any particular lot of seeds.<sup>3</sup> This would indicate that, although the tendency to produce nucellar embryos is inherited, the environment may materially influence the number of such embryos actually developed under any particular set of conditions. This tendency to produce supernumerary nucellar embryos is a serious handicap to any effective study of progeny in citrus-breeding experiments. The observation with reference to the variability in the number produced, however, pointed to a possible method of solving the problem. A working hypothesis was formulated on this basis and definite experiments initiated to test it.

The original hypothesis, formulated in 1932, was that the initiation of such nucellar embryos might be inhibited or that such embryos might be rendered inactive or destroyed after formation by decreasing the food supply ("starving" the entire pericarp). Since 1932 the hypothesis has been amplified as to the nature of the environmental factors which may be operative—the nature and amount of food supply, moisture supply, temperature, age of seed, seed maturity, desiccation of seed, etc.

The specific method used in the initial attempts to decrease the food supply available to the developing pericarp was to keep it and the surrounding leaves covered until maturity with three thicknesses of cheese-

<sup>1</sup> E. Strasburger, *Zeitschr. f. Naturwiss.*, 12: 654-678, 1878.

<sup>2</sup> L. W. Sharp, "An Introduction to Cytology," 2nd Ed., 1926.

<sup>3</sup> H. J. Webber, *Hilgardia*, 7: 1-79, 1932; *Calif. Agr. Expt. Sta. Bul.*, 317, 1920; *Jour. Hered.*, 11: 291-299, 1920. Howard B. Frost, *Hilgardia*, 1: 365-402, 1926. H. J. Toxopeus, *Landbouwk. (Buitenzorg) Jrg.*, 64: 1930-31.