The Pineal Gland in Relation to Somatic, Sexual and Mental Development

CAREY PRATT McCORD, M.D.
DETROIT
From tumors involving the pineal gland, two distinct systems of symptoms and signs ensue, the neurologic and the metabolic. The neurologic manifestations arise from the encroachment of the neoplasm on the intracranial contents and are indications of changes in pressure, in placement and of destruction of tissue. Such changes are the consequence of pineal tumors at any age of the patient; but in pineal tumors appearing in prepuberal life a second group of changes arise, the metabolic. These metabolic alterations are referable to disturbance in the gland's secretory function. Apparently only in young males is this syndrome complete. It consists of (1) early sexual development evidenced in the enlarged sex organs, pubic hair, general body hair, early changes in voice; (2) precocious mental development evidenced in the maturity of thought and speech, and (3) general body overgrowth to the extent that a child of 5 or 6 years may have the appearance of a child of 11 or 12.

A case reported by Machell presents these changes in a striking manner. The patient was a boy less than 6 years old at the time of the publication. At the age of 5 months there was pubic hair, erections at 17 months, emissions at 30 months. The patient's weight was 7½ pounds above normal at 4 months of age, 12 pounds in excess at 8 months, 20 pounds in excess at 3 years. When the patient was 44 months old, his height was 8½ inches above normal for a child of that age.

* Read before the Section on Pathology and Physiology at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.
1. For review of clinical cases see Bailey, Pearce, and Jelliffe, Smith Ely: Tumors of the Pineal Body, Arch. Int. Med., December, 1911, p. 851. For Physiology and Anatomy, see Vincent Swale: Internal Secretion and Ductless Glands, 1912.
At 48 months the circumference of the head was over 2 inches in excess of normal. The voice was a deep bass. Mental precocity was very marked and the general bearing and language was that of a much older person.

On account of the difficulties attending experimentation on this vestigial organ, the clinical findings with subsequent necropsy records have been the prime factor in the formulation of the prevailing ideas as to this gland's functions. The conception of this gland's function, however, has in part been developed from laboratory studies, notably from the results concomitant with the extirpation of the organ. This has been attempted frequently, but the situation of the gland is such that in the greater number of instances death followed the operative procedure, from hemorrhage or injury to the vermis or the occipital lobes. By operating on a large number of animals some workers have had a few animals survive. No changes attended the removal of the gland by Biedl, Dandy and Exner and Boese, but Foa ablating the gland in chicks and Sarteschi in young rabbits and puppies report the production of the precocious macrogénitosomatic syndrome.

The general plan of work entailed in this study has been to feed to very young animals minute quantities of pineal tissue and to record the weight changes, sexual differences, and in the case of dogs increased mentality, over control animals maintained under otherwise identical conditions. One hundred and ten guinea-pigs, eighteen puppies, fourteen adult dogs and sixteen chicks have been under observation.

Fresh pineal glands from cattle have been employed. These were in part from veal, in part from young adults approximating 3 years, and in part from the general run of cattle from the abattoirs. The glands averaged in weight (on weighing sixty glands) 2.14 grams. There were in the many thousand glands making up the several pounds that have been used, marked variations in size, shape and melanopigment. This pigment, which was present in a high percentage of glands, involves chiefly the encapsulating tissue.

For feeding experiments the glands were prepared for permanent use in the following manner: The fresh glands were rinsed free of blood and stripped of adherent tissue. They were ground to a fine paste in the Latapie grinder, and without drying, the paste was admixed with milk-sugar in such quantity that ½ grain milk-sugar represented 10 mg. pineal tissue. The mass was made into ½-grain tablets and quickly dried at room temperature.

Early in the work it was apparent that the more striking results were being obtained from the animals fed with pineal substance from cattle not having reached adult life. Efforts were then made to establish quantitatively the activity and the identity of the various experimental lots of pineal preparations by

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employing the methods commonly used in testing the activity of endocrinous derivatives. Although certain cardiovascular changes regularly follow the intravenous administration of pineal extracts to dogs, the extent of these changes is not a measure of the activity of the gland as a stimulator of growth.

On the hypothesis that precocious development is due to hypopinealism, the first work was done in anticipation that feeding would retard development and prolong the presexual life. This was begun on two chicks incubated in the laboratory. Beginning at the age of two days one was fed 10 mg. veal pineal tissue, three times weekly, the other (and in all cases of controls) was fed a blank tablet of milk-sugar. The difference in growth should be noted (Table 1).

![Fig. 1.—Position, relations and relative size of the pineal gland. Taken from beef 3 years of age.](image)

### Table 1.—Results of Feeding Pineal Gland to Chicks

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>3rd</td>
<td>319.5</td>
<td>92.5</td>
<td>227.0</td>
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<tr>
<td>6th</td>
<td>557.7</td>
<td>286.5</td>
<td>271.2</td>
</tr>
<tr>
<td>9th</td>
<td>895</td>
<td>550</td>
<td>345</td>
</tr>
<tr>
<td>12th</td>
<td>923</td>
<td>700</td>
<td>223</td>
</tr>
</tbody>
</table>

The striking disproportion in size and the marked skeletal overgrowth, making the large chick very awkward in his movements, soon made these chicks a laboratory curiosity, but the small number and the different sex did not justify any inference as to the influence of the pineal feeding. The results, however, were so striking that at once work was instituted in a more extensive way.

A lot of fifty guinea-pigs in the second week of life was selected and divided into test and control groups. The test pigs were fed daily 10 mg. veal pineal tissue. The controls were fed a ½-grain milk-sugar tablet. Other conditions for the two lots were identical. The results obtained are given in Table 2.

### Table 2.—Results of Feeding Pineal Gland to Young Guinea-Pigs

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1</td>
<td>198.7</td>
<td>-2.5</td>
</tr>
<tr>
<td>2</td>
<td>230</td>
<td>21.3</td>
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<tr>
<td>3</td>
<td>256.8</td>
<td>6.8</td>
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<td>4</td>
<td>251</td>
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<td>10.9</td>
</tr>
<tr>
<td>10</td>
<td>336.5</td>
<td>46.3</td>
</tr>
</tbody>
</table>

Average weight at end of tenth week... 410.8 gm. Average initial weight... 204.3 gm.

Average gain... 155.4 gm. Gain, per cent... 76.0

Excess gain of pineals over controls, 23 per cent.
This excess in weight of pineal-fed guinea-pigs over their controls is a symmetrical overgrowth. There is some increased adipose tissue, but this is generally distributed and not localized in any one region of the body. At no time has it been possible to continue this excessive growth above normal adult size. As the animals approach adult size the pineal feeding is less effective and after full maturity is attained is without effect. There has been no tendency to gigantism.

As a step toward determining the metabolic differences, quantitative urinalyses were made on twenty-four-hour composite samples of urine from the two groups. 0 With proper regard for the numerous other factors that might vitiate the results obtained from urinalyses, there is a suggestive difference in the two urines as may be seen in the summary given in Table 3.

**TABLE 3.—SUMMARY OF ANALYSIS OF URINES**

<table>
<thead>
<tr>
<th></th>
<th>Pineal</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total volume collected (24 hours)</td>
<td>187 c.c.</td>
<td>169 c.c.</td>
</tr>
<tr>
<td>Specific gravity (15.5 C.)</td>
<td>1.016</td>
<td>1.019</td>
</tr>
<tr>
<td>Total solids</td>
<td>2.51</td>
<td>3.02</td>
</tr>
<tr>
<td>Water</td>
<td>97.49</td>
<td>96.98</td>
</tr>
<tr>
<td>Total mineral matter</td>
<td>1.21</td>
<td>1.37</td>
</tr>
<tr>
<td>Total nitrogen</td>
<td>0.825</td>
<td>0.825</td>
</tr>
<tr>
<td>Total creatinin</td>
<td>0.018</td>
<td>0.025</td>
</tr>
<tr>
<td>Phosphoric acid (as P₂O₅)</td>
<td>0.016</td>
<td>0.043</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.018</td>
<td>0.018</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.018</td>
<td>0.018</td>
</tr>
<tr>
<td>Alkalinity (as Na₂CO₃)</td>
<td>0.013</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Chicks.—A lot of fourteen chicks was secured at the age of one week. At so early an age sex could not be determined and the lot was divided into test and control groups without knowledge as to grouping by sex. The test chicks were placed on veal pineal tissue for one week with a resultant greater growth than controls. For the next four weeks they were fed pineal tissue from old cattle, without gaining. On being placed on the original veal preparation the test chicks again grew in excess over controls.

Dogs.—The eighteen dogs employed represent four litters. Infection of these puppies with distemper interfered seriously with the weight charts of these animals. So long as infections could be kept out of the animal quarters, the test animals outgrew the controls, but the wasting from infections interfered seriously with average results over prolonged periods. It was in connection with puppies that some differences in intelligence were observed. No great import is attached to these observations, but it was noted that the pineal-fed dogs were about one month ahead of the others in their habits. They were the first to learn to lap milk, the first to respond to a call, the first to be able to find their way back to the kennel. When work on these animals was discontinued, only the pineal-fed animals were in demand as pets, and those choosing them did so without any knowledge as to

9. I am under obligations to Mr. Lewis Davis for these analyses.

males and females of each group were then placed together in breeding-pens. As a measure of any difference in sexual development it was thought desirable to note the date of birth of young in the two lots. As the end of the approximate gestation period approached, these animals were observed as to the date of giving birth to young. All except two of the pineal-fed pigs gave birth to young before the first of the controls. Fourteen days elapsed between the birth of young of the first pineal-fed pig and the first control pig. In all cases the young were normal and in no wise different from any other young pigs.

COMMENTS AND SUMMARY

In the foregoing records of experiments, it may be observed that some of the changes generally attributed to deficiency of pineal secretion may be produced by supplying an added amount of pineal substance. In an effort to reduce to rationality these identical findings derived from two opposing sources, the so-called destructive neoplasms of the pineal gland on the one hand, and the feeding of the gland on the other, there arise two possibilities: First, this syndrome may appear from disrupting the general endocrinous balance from either increasing or decreasing the amount of pineal secretion available for the body's use. These secondary changes in the other endocrinous glands are now in the course of investigation. Second, the cells of the neoplasms involving the pineal gland may retain some of the metabolic and other functional characteristics of the normal pineal cell from which they were derived, and the peculiar body, sexual and mental changes in patients with such tumors are all manifestations of increased rather than decreased pineal activity. One of the most frequently occurring lesions of the pineal is the adenoma, and there is abundant evidence that at times cells of adenoma functionate after the manner of the cells from which they arise. In adenoma of the liver in cases reported by Weber,11 Rolleston,12 Wheeler13 and Ribbert,14 distinct bile secretion by tumor-cells has been pointed out. Ribbert established that the bile present in such tumors was not the bile of icterus from necrotic liver-tissue by demonstrating that the scirrhous encapsulating tissue was free from bile-stain and that the bile was confined to the liver-like cells of the active tumor. In at least one case, a metastasis in the lung from the liver secreted bile. In this connection it is significant that the functioning glandular cells of typical thyroid structure have been found in thyroid metastases in bone-tissue. Furthermore, in myeloma of the bone-marrow the cytoplasm15 of the tumor-cells contain the granules that characterize normal myelocytes, that is, the tumor to a certain extent assumes the function of the bone-marrow. All considered, it is perceived that functional activity of tumor-cells is not infrequent. germane to the present contention is the statement by Hinds Howell16 in describing the characteristics of the cells of the pineal tumors of his three cases. He says:

A noteworthy feature is the similarity of these tumor-cells in many instances to those of the normal pineal gland.

The results of this work lead me to the conclusion that the administration of minute quantities of pineal tissue from young animals to young animals stimulates rapid growth of the body, but not beyond normal size. Also there are less well-established indications of precocity of mental and sexual development.

Fig. 3.—Effect on growth of guinea-pigs produced by feeding pineal-gland tissue. Control pigs to left, test pigs to right.

The Pineal Gland in Relation to Somatic, Sexual and Mental Development

Second Paper

CAREY PRATT McCORD, M.D.
DETROIT
Current descriptions of the pineal gland attribute to this organ the function of producing a secretion which inhibits growth of body and restrains mental and sexual development from exceeding the rate looked on as normal for preadult life. This inference arises from the occasional distinctive precocity of development following invasion of the pineal gland by neoplasms. It is assumed that such neoplasms destroy the gland, and that any resulting metabolic disturbances occur from the deprivation of the body of the pineal's elaborated substances.

From a reactionary point of view, the groundwork for such a theory is both meager and unstable. From sixty-five to seventy authentic cases of pineal tumors have come under observation. These have been distributed over more than a century. Copies of the original descriptions are rarely readily accessible. By reason of faulty translations and inaccuracies in quotations, some descriptions of pineal gland syndromes have come to resemble classical myths. Of the sixty-five to seventy cases, only about 10 per cent. present those striking effects characterized as the "precocious macrogenitosomatic pineal syndrome." The instances of greatest metabolic disturbances have occurred in persons below 14 years of age. Of the total number of cases, sixteen were recognized before the age of 14 was attained—twelve boys and four girls. The syndrome has appeared in more striking form in boys than in girls, but the ironclad statement that the syndrome is confined to males is probably unwarranted. Marburg's case in a girl of 9 presents metabolic altera-
ations equally as striking as those in boys cited as types of the pineal syndrome. It is noteworthy that the pineal syndrome has occurred only in such cases of pineal tumors as have led to an obstructive hydrocephalus and thus, of necessity, to secondary hypophysial disturbances (Cushing).

In the remaining of the total sixty-five to seventy pineal cases, there appear various departures from the established syndrome. The greater number, whether adults or children of either sex, manifest no metabolic disturbances attributable to pineal functional perversion. The nicety of the theory that only in childhood and only in boys does this syndrome appear, is apparently jeopardized by the occurrence of pineal tumors with adiposity in adults of both sexes, with adiposity and infantilism in both sexes, and with cachexia. In part, these deviations from anticipated findings are due to secondary involvement of others of the endocrinous system, notably the hypophysis. The interrelation with others of the glandular system has been emphasized by Marburg, Fränkl, Hochwart and others, but in some instances, the necropsy demonstration of a pineal tumor led to the crediting of all prior changes to pineal dysfunction.

The available histories frequently do not permit a restudying in the light of later developments in our knowledge of the interrelation of the several glands. When this is possible, many of the apparent discrepancies and conflicts are rendered more nearly harmonious through evidence of involvement of other glands, especially the hypophysis, and secondary to it the sex organs. When, however, a delineation is made of the extent of these secondary influences and these are hypothetically set apart, there still remain alterations probably attributable only to primary pineal dysfunction. The complete syndrome is characterized by (1) overdevelopment of the sex organs, both anatomic and functional; (2) precocity of mental development; (3) general overgrowth of body with or without adiposity — the whole picture being one of early maturity. The syndrome is rarely complete. The most nearly complete cases have occurred in boys below or near 7 years of age. It is at this age rather than at puberty that the gland presents its greatest histologic evidence of a beginning involution.

A second pineal syndrome whose essential feature is cachexia has been described. This is much less definitely connected with pineal dysfunction, and has been more especially associated with the occurrence of tumors in adult life. It is described as representing apinealism.

The nature of the pineal syndrome, whether it be the outgrowth of hyperpinealism or hypopinealism, or whether a clinical condition corresponds to each of these deviations from normal, is not established. On the recognition of a specific pineal syndrome (or syndromes), efforts were made to establish its cause by reproducing the condition in animals through the experimental removal of the gland. The gland's extirpation is difficult, but has been successfully performed in both young and adult animals. The results are rendered less authoritative by the vitiating effects of the trauma necessary in the gland's removal. Pinealectomy determined no changes that might be associated with pineal functions as observed by the majority of investigators. Foa and Sarteschi, respectively, report that, of the animals which survived the operative procedures, some young males evinced certain features of the pineal syndromes. The similarity on comparison with clinical cases is remote.

The precocious macrogenitosomatic syndrome is usually ascribed to hypopinealism. The theory suggested above as current assumes that pineal lesions are destructive, and that concomitant metabolic disturbances arise from the lack of pineal secretion. To the contrary, running through the publication of a number of observers are to be noted suggestions that pineal neoplasms retain some of the functional characteristics of normal pineal cells, and that the pineal syndrome is due to increased rather than decreased function of the gland. The similarity of pineal tumor cells to normal pineal cells has been pointed out by Howell. The retention of function in neoplasms in other glands is not infrequent; tumors in the hypophysis have in a number of cases occasioned acromegaly, a hyperpituitarism; tumors of the thyroid and metastases from thyroid tumors may secrete typical thyroid colloid; suprarenal gland neoplasms yield the active prin-

ciple of the normal suprarenal; bile is secreted by cer-
Askanazy. However, the evidence used by Marburg may lead to an active constructive stimulating influ-
ence (hyperpinealism) is suggested in publications by Marburg,2 Oestreich and Slawyk4 and Askanazy.6 However, the evidence used by Marburg may readily be turned to support the idea of hypo-
physial involvement in his case. Oestreich and Slawyk regard the early sexual maturity as hyperpinealism analogous to acromegaly from hyperpituitarism. Askanazy suggests that teratomas may be regarded as “false conceptions,” in which one might expect, pri-
amarily at least, an increase in the pineal secreting functions (compare Bailey and Jelliffe). It is note-
worthy that the best-defined cases of pineal syndromes regularly occur from pathologic conditions invading the actual tissue of the gland, rather than from simple cysts and from adjacent tumors involving the pineal only by compression.

In this rather uncertain situation, it is held that, in case uniform and consistent manifestations followed the experimental administration of pineal gland tissue, and these manifestations stood in some qualitative relation to evidence as to function derived from other sources, such experiments, rigidly controlled, would be acceptable as bearing on the functions of the gland. Accordingly, such experiments have been performed. The results have been indicated in part in a prelimi-
ary report.6 A report of results from a continuation of this earlier work constitutes the remainder of this paper.

EXPERIMENTAL DATA

Feeding experiments with small animals, in which the results were measured in such terms as weight dif-
ferences and body disproportions, are so vitiated by trivial differences in the living conditions of the experi-
mental and control animals that any deductions should be made most guardedly. The findings from a single series of feeding experiments might easily be misin-
terpreted because of some deleterious influence of obscure origin. When, however, the investigation includes a number of series of animals, and the different series are maintained under varied experimental conditions, no accidental influence would constantly be exerted on a single phase of the experimentation. Any deviations from the normal, regularly appearing in the several experimental groups, may be attributed to the influence of the substances employed in feeding.

Because of this facility with which abstruse errors enter into feeding experiments, the preliminary work, which included results from feeding chicks, guinea-pigs and puppies, has been extended to include results from 393 animals. Variations have been introduced, in dosage, in method of administration, in source of material used (species and age of animals supplying glandular material) and in age of test animals. Except for one series of experiments on the influence of the pineal on embryonic development, guinea-pigs have been exclusively employed as test animals.

THE INFLUENCE OF PINEAL GLAND ADMINISTRATION AS SEEN IN WEIGHT DIFFERENCES

(a) Effect of feeding the pineal substance from old adult cattle to young animals.

Series A (forty-eight young pigs, aged 2 weeks, an equal number of males and females, sexes maintained apart) was equally divided into control and experimental lots. To the experimental lot, 10 mg. of pineal tissue from adult cattle was daily administered by mouth. The controls were simi-
larly given a corresponding amount of inert material. This was continued ten weeks with weekly weighings. Since to the pineal are attributed functions confined to preadult life, it might be anticipated that feeding with mature glandular material would cause no change. On the other hand, the histologic picture of the adult pineal indicates the persistence of some glandular elements throughout life. The two lots of animals under observation as to this point ran essentially parallel weights. At the end of the ten weeks, the experi-
mental animals had gained on an average of 130.5 per cent., while the controls gained 136.5 per cent.

As a check on Series A, Series G was similarly carried out with results as indicated in Table 1.
Comparing Results

Wherever it has been possible to induce a rapid body growth, feeding has, at no time, been a tendency toward gigantism. This excessive growth is of the same age is shown in Table 2.

In Series E and E, another variation was introduced by the substitution of lamb pineal tissue for that of veal and cattle. The gland in lambs is of different shape from that found in cattle. The lamb gland is round instead of oval, the melanin pigment is (when present) localized in the distal portion. The lamb glands weigh, on an average, 100 mg. The method of preparation of this tissue was the same as that earlier described. Such material was administered to the animals of Series E in 10 mg. amounts daily. The results are indicated in the general tabular summary. To E, 100 mg. of the same tissue was administered. This larger dose was evidently not well borne by the alimentary tract, for, during the eleven weeks of feeding, there were irregular periods of distinct loss of weight. Ultimately, however, an excess of 40.9 per cent. was determined as the gain of pineal fed over control animals.

(b) The effect of administering veal pineal glands to old experimental animals.

The counterpart of the foregoing experiments was also undertaken. All earlier experiments in which the work was begun with young animals, but continued to the time of adult life, contribute data to this present phase of inquiry. Wherever it has been possible to induce a rapid body growth in immature animals, it has never been possible to continue this excessive growth above normal adult size. As the animals approach adult size, the pineal feeding is less effective, and after full maturity is reached, is without effect. There has, at no time, been a tendency toward gigantism.

Male guinea-pigs are sexually active before 4 months, and at 6 months are considered mature adults. However, these bucks subsequently slowly increase in size for several months before attaining their maximum weight. Series F (all males) was directed toward this period of growth. The animals were picked at 6 months of age, fed veal pineal tissue, and controlled as in other reported series. The feeding was maintained for four weeks, but weighings were continued for eight weeks. In this period the average experimental buck gained 167.6 gm., while the average control gained 121.4 gm.

(c) The effect of administering pineal glands from young animals to young experimental animals.

The greater portion of the data of the original paper is directed toward this phase. Of the more recent work, Series C, D, E and E, (hereinafter described, Table 3) contribute data.

In Series C, D, E, and E, where it has been possible to induce a rapid body growth, feeding has, at no time, been a tendency toward gigantism. This excessive growth is of the same age is shown in Table 2.

In Series E and E, another variation was introduced by the substitution of lamb pineal tissue for that of veal and cattle. The gland in lambs is of different shape from that found in cattle. The lamb gland is round instead of oval, the melanin pigment is (when present) localized in the distal portion. The lamb glands weigh, on an average, 100 mg. The method of preparation of this tissue was the same as that earlier described. Such material was administered to the animals of Series E in 10 mg. amounts daily. The results are indicated in the general tabular summary. To E, 100 mg. of the same tissue was administered. This larger dose was evidently not well borne by the alimentary tract, for, during the eleven weeks of feeding, there were irregular periods of distinct loss of weight. Ultimately, however, an excess of 40.9 per cent. was determined as the gain of pineal fed over control animals.

(d) Difference in effect of pineal administration on animals of different sex.

The pineal clinical syndrome has been best established in males. In extirpation experiments, only in males have metabolic disturbances been described. Because of this
apparent predilection for males, the results of feeding have
been analyzed for data as to the relative responsiveness of
the two sexes. Series E and a part of B have been analyzed.
Early it was obvious that both males and females responded
to pineal stimulation. It was anticipated that the
early gains of experimental males over control males in compari­
sion with gains of experimental females over control females.
On such a basis, two thirds of the excess gains are made by
males. This was observed in Series E, in which the
total period determined a general excess of 19.3 per cent. in
favor of experimental animals. Analysis of this gain by sex
indicates a 25.8 per cent. gain for the males, and for the
females, 12.7 per cent. Details of the analysis of Series B are
given in Table 4.
(e) Summary and comment on weight differences.
The data accruing from two years of feeding experiments
with pineal substance are sufficiently extensive to free the
results of accidental vitiating factors. Averages of a
number of experimental series aggregating nearly 400 animals
would indicate that young animals to which had been admin­
istered pineal tissue developed at a rate in excess of normal
controls.
The most pronounced results arose from the feeding of
young animals with material derived from young animals.
Although some histologic evidence exists indicating the
glandular nature of the pineal in mature adult life, such
material, when fed to young animals, did not bring about
the changes observed in feeding with younger pineal
material.
At no time has gigantism been produced. As adult life
is approached, pineal feeding is less effective.
The excess growth of young animals under pineal feeding
is grossly symmetrical. No disproportion has been observed
except a possible hypertrophy of the testes noted in some
animals. In microscopic sections, such testes are seen to
be made up of larger and more mature tubules than in controls
of the same age, but with no increase in the interstitial
tissue.
Both males and females are affected by pineal administra­
tion, but the gains (in relation to respective controls) have
been greater for the males than for females.

TABLE 3.—PERCENTAL GAINS OF VARIOUS SERIES DURING
SIX WEEKS’ GROWTH

<table>
<thead>
<tr>
<th>Series</th>
<th>Second Week</th>
<th>Fourth Week</th>
<th>Sixth Week</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Pineal</td>
<td>Control</td>
</tr>
<tr>
<td>B</td>
<td>20.9</td>
<td>27.9</td>
<td>27.5</td>
</tr>
<tr>
<td>C</td>
<td>28.0</td>
<td>26.6</td>
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<tr>
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<td>27.7</td>
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<tr>
<td>E</td>
<td>29.5</td>
<td>26.8</td>
<td>40.5</td>
</tr>
<tr>
<td>F</td>
<td>27.7</td>
<td>26.9</td>
<td>47.9</td>
</tr>
</tbody>
</table>

Averages of a number of experimental series aggregating nearly 400 animals would indicate that young animals to which had been administered pineal tissue developed at a rate in excess of normal controls.

The most pronounced results arose from the feeding of young animals with material derived from young animals. Although some histologic evidence exists indicating the glandular nature of the pineal in mature adult life, such material, when fed to young animals, did not bring about the changes observed in feeding with younger pineal material.

At no time has gigantism been produced. As adult life is approached, pineal feeding is less effective.

The excess growth of young animals under pineal feeding is grossly symmetrical. No disproportion has been observed except a possible hypertrophy of the testes noted in some animals. In microscopic sections, such testes are seen to be made up of larger and more mature tubules than in controls of the same age, but with no increase in the interstitial tissue.

Both males and females are affected by pineal administration, but the gains (in relation to respective controls) have been greater for the males than for females.

The influence of pineal feeding on sexual maturity

Of any several groups of premature guinea-pigs maintained under normal conditions, it is assumed that individuals will attain to sexual maturity near the same time and will give birth to young at about the same subsequent time. In case of a regularly recurring marked difference in time of birth

TABLE 4.—ANALYSIS OF GAINS BY SEX (Series B)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Control, 2 Weeks Old</th>
<th>Pineal, 2 Weeks Old</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>1</td>
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</tr>
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<td>4</td>
<td>20.0</td>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>14</td>
<td>20.0</td>
<td>19.9</td>
</tr>
</tbody>
</table>

Excess pineal males over control males.............. 7.4 per cent.
Excess pineal females over control females........ 10.2 per cent.

of first young in one phase of an experimental lot of animals, it is rational to associate this phenomenon with different times of attaining to maturity. On such a basis it has been noted in all groups of animals which were allowed to breed that the pineal-fed mothers gave birth to young earlier than the controls. One series including forty-five animals was carefully conducted with a view to any data bearing on the matter in question. The two sexes were kept together from birth. The feeding with veal pineal tissue was continued for fourteen weeks. During this time the pineal-fed attained to a size 32 per cent. larger than their controls of the same
ages. The female farthest advanced in pregnancy among the pineal-fed animals aborted, so that the date of birth of first young was not determined. The first normal birth occurred July 3 in the experimental group. Others of the same group followed until over half the females had given birth to young. Then three weeks and two days later, July 26, the first control pig was born. The progeny in all instances were like any other pigs. After all pigs were born in both groups and after an interval of several weeks, the same females were placed with normal bucks to detect a possible difference in the second pregnancy. No such difference was detectable.

GENERAL SUMMARY

From the foregoing experiments, evidence of the precocity of development usually attributed to pineal deficiency (hypopinealism) has been obtained in animals by supplying an increased amount of pineal substance by feeding or injecting pineal preparations. Such administration of pineal substances led to a more rapid growth of body than normal, and determined an early sexual maturity. The excess in rate of growth was most pronounced (40.9 per cent. excess in eleven weeks) in young animals fed with pineal tissue obtained from young animals. No tendency to gigantism has followed pineal administration. After maximum size was attained, pineal administration appeared to be ineffective. Both males and females respond to the influence of pineal substances in rate of growth, but the response has been more definitely manifested in males.

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