

EXTIRPATION OF THE PINEAL BODY.

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PLATES 29 TO 36.

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The pineal body until recently has been regarded merely as a very curious vestigial inheritance, serving in the chain of evolution as a reminder of a far distant functioning pineal or central eye. There seems to have been nothing in its macro- or microscopic appearance sufficiently noteworthy to stimulate the especial interest of either anatomists or physiologists. Its inaccessible location has, perhaps, deterred experimenters from undertaking investigations of apparently so little promise.

Tumors of the pineal had not infrequently been reported by pathologists, but there was nothing which seemed significantly correlative in the pathological findings and the clinical signs and symptoms. The marvelous story of the thyroid, parathyroids, hypophysis, and adrenals is, no doubt, largely responsible for the recent endeavors to promote the pineal to a position of like importance among the endocrine glands.

In 1898 Heubner¹ presented a case of markedly precocious sexual and less pronouncedly precocious somatic development. The patient was a boy of 4½ years with pubic hair 1 cm. long, penis and testicles as large as the normal at puberty. The mammæ were conspicuous. The body development was equal to that of a boy of 8 or 9. He was abnormally fat. A diagnosis of tumor of the hypophysis was made. The following year this case was reported by Oestreich and Slawyk,² who found at autopsy a teratoma of the pineal. Almost

¹ Heubner, *Allg. med. Centr.-Ztg.*, 1899, lxxviii, 89.

² Oestreich, R., and Slawyk, *Riesenwuchs und Zirbeldrüsen-Geschwulst*, *Virchows Arch. f. path. Anat.*, 1899, clvii, 475.

simultaneously Ogle³ reported a very similar case, a boy of 6 years with precocious sexual development. The precocity was principally evidenced by an enlarged penis and the presence of pubic hair. The testicles were about normal in size. In this instance also a teratoma of the pineal was found post mortem.

Marburg,⁴ in 1907, collected from the literature about forty cases of pineal tumor and added a case of his own. Marburg's patient presented no precocity either sexual or somatic; he was merely too fat. Marburg endeavored to establish a pineal clinical entity, and ventured even to pronounce upon the degree, in a given case, of the activity of this gland. He classified all pineal glandular symptoms under the three heads, hypopinealism, hyperpinealism, and apinealism. Hypertrophy of the genitals and precocity were found in hypopinealism, adiposity in hyperpinealism, and cachexia in apinealism.

According to this conception, the pineal and pituitary would seem to have antagonistic activities. Hypertrophy of the pineal is expected to produce an adiposity indistinguishable from Fröhlich's dystrophia adiposogenitalis of hypopituitarism. Atrophy of the pineal would be accompanied by genital and somatic hypertrophy and precocity, whereas acromegaly results from hyperplasia of the pituitary gland. Cachexia is described with both apinealism and apituitarism.

It was Marburg's view that the pineal, normally functioning only during the early years of life, inhibited genital and somatic growth and sexual characteristics, and that its partial destruction by tumors with the resultant hypopinealism permitted, uncontrolled, the development of these features. Consequently, tumors in older youths and adults would not cause sexual abnormalities, because the pineal in them had ceased to function. This view is in accord with the anatomical evidences of its involution after the early years of life.

³ Ogle, C., (1.) Sarcoma of the Pineal Body, with Diffused Melanotic Sarcoma of the Surface of Cerebrum. (2.) Tumor of Pineal Body in a Boy, *Tr. Path. Soc. London*, 1898-99, 1, 6.

⁴ Marburg, O., Zur Kenntnis der normalen und pathologischen Histologie der Zirbeldrüse; die Adipositas cerebri, *Arb. a. d. neurol. Inst. a. d. Univ. Wien*, 1908, xvii, 217; Die Adipositas cerebri. Ein Beitrag zur Pathologie der Zirbeldrüse, *Wien. med. Wchschr.*, 1908, lviii, 2617.

It must be emphasized that at the time of Marburg's publication there had been absolutely no significant experimental investigations on the pineal and that his classification is based solely on clinicopathological observations; also that of about forty cases of tumor of the pineal gland only in the two above mentioned instances was there any sexual, somatic, or mental precocity. In several cases varying degrees of adiposity had been noted. It is also worthy of note in passing that in both cases of sexual precocity the tumor was a teratoma.

Since Marburg's publication many cases of pineal tumor have been added, the total now being about sixty cases. Von Frankl-Hochwart's⁵ case, also a teratoma of the pineal, in a boy of 5½ years, rather large for his age, showed sexual hypertrophy and precocity two months before death. The patient developed a deep voice and the genital hair was equal to that of a boy of 15. There was also mental precocity. Raymond and Claude⁶ added a case which presented increasing adiposity, and somatic development but without sexual changes. With the exception of a rather frequent adiposity the other cases have shown but little to indicate glandular influences.

Experimental work has since been added but with contradictory results. In general, attempts have been made to reproduce so called hyperpinealism by feeding pineal extract and apinealism or hypopinealism by extirpation of the pineal. In feeding experiments by McCord⁷ on guinea pigs, chickens, and dogs, an increase in weight together with earlier sexual maturity and sexual characteristics resulted. Dana and Berkeley⁸ fed pineal extract of young bullocks and calves to guinea pigs, rabbits, and kittens, and noted a 25 per cent increase in weight over the controls. Later fifty children were injected with pineal extract, but they grew in height and weight

⁵ von Frankl-Hochwart, L. Über Diagnose der Zirbeldrüsentumoren, *Deutsch. Ztschr. f. Nervenhe.*, 1909, xxxvii, 455.

⁶ Raymond, F., and Claude, H., Les tumeurs de la glande pinéale chez l'enfant, *Bull. de l'Acad. de méd. de Paris*, 1910, lxiii, series 3, 265.

⁷ McCord, C. P., The Pineal Gland in Relation to Somatic, Sexual and Mental Development, *Jour. Am. Med. Assn.*, 1914, lxiii, 232.

⁸ Berkeley, W. N., Dana, C. L., Goddard, H. H., and Cornell, W. S., The Functions of the Pineal Gland, with Report of Feeding Experiments, *Med. Rec.*, 1913, lxxxiii, 835. Dana and Berkeley, The Functions of the Pineal Gland, *Month. Cycl. Pract. Med.*, 1914, xxviii, 78.

less rapidly than the controls, though a distinctly greater mental improvement was observed. These observers think there is no doubt that injections of pineal will clear low grades of mental deficiency. These claims are quite similar to those of McCord, who noted mental precocity in his pineal-fed puppies.

Attempts have been made to remove the pineal by Exner and Boese,⁹ Foà,¹⁰ and Sarteschi.¹¹ The results of these investigations add even more confusion. Exner and Boese found absolutely no changes following complete or partial removal of the pineal. Sarteschi found adiposity, greater somatic and genital development, and sexual precocity in young dogs. Following extirpation of the pineal of chickens, Foà observed a premature development of the primary and secondary sexual characters.

Briefly, therefore, adiposity may result by feeding pineal extract (McCord, Dana, and Berkeley) or by complete or partial removal of the pineal (Sarteschi). Sexual and somatic precocity may result from feeding pineal extracts (McCord, Dana, and Berkeley), or from partial or complete removal of the pineal body (Foà, Sarteschi), or nothing may result from its partial or complete destruction (Exner and Boese). Such is the paradoxical experimental support for Marburg's hypothesis of pineal function.¹²

The foregoing is presented as a purely objective, concise summary of our present knowledge of the pineal. A detailed consideration of the clinical and experimental observations will be given in a subsequent communication. The purpose of this paper is to report briefly the results of pinealectomy in a series of young puppies

⁹ Exner, A., and Boese, J., Ueber experimentelle Exstirpation der Glandula pinealis, *Deutsch. Ztschr. f. Chir.*, 1910, cvii, 182; Ueber experimentelle Exstirpation der Glandula pinealis, *Neurol. Centralbl.*, 1910, xxix, 754.

¹⁰ Foà, C., Ipertrofia dei testicoli e della cresta dopo l'asportazione della ghiandola pineale nel gallo, *Pathologica*, 1911-12, iv, 445.

¹¹ Sarteschi, U., La sindrome epifisaria "macrogenitosomia precoce" attenuata sperimentalmente nei mammiferi, *Pathologica*, 1913, v, 707.

¹² It should also be noted that Pellizzi (Pellizzi, G. B., La sindrome "macrogenitosomia precoce," *Neurol. Centralbl.*, 1911, xxx, 870), in 1910, presented two cases of somatic and sexual precocity without substantiation of the diagnosis, as cases of "la sindrome epifisaria macrogenitosomia precoce." In the absence of anatomical proof and the rarity of a correct clinical diagnosis of pineal tumor, this evidence can not be accepted. It was in Pellizzi's laboratory that the experimental work of Sarteschi was conducted.

and to describe the method which has been evolved for extirpation of the pineal body.

Experimental Removal of the Pineal.

In the higher mammals the pineal is so deeply situated, so minute, and so intimately associated with important and easily injured structures that its removal by operation has been regarded as impractical. It is covered by the splenium of the corpus callosum and by the vena Galena magna. It lies between the anterior corpora quadrigemina, and consequently is just above the aqueduct of Sylvius. It is situated almost exactly in the center of the brain. Its removal necessitates opening the third ventricle, the posterior wall of which it forms a part. The greatest of the dangers encountered in the removal of the pineal is hemorrhage, and especially hemorrhage into the ventricles. The greatest difficulty is the definite recognition of the gland.

Foà has successfully excised pineals from chickens, but with the exception of Sarteschi's work, the removal of the pineal in higher mammals has not been successful. Exner and Boese attempted its removal in dogs but soon yielded to the more expedient but objectionable method of cauterization. By these investigators the cautery was inserted blindly through a trephine opening in the skull. This procedure was accompanied by a very high mortality. From a series of 95 animals, death resulted from the operation in 75. The principal cause of death was hemorrhage. This is not surprising, since a successful introduction of the cautery must almost necessarily perforate the vena Galena magna. Sarteschi's operative results were almost equally disastrous. Of 15 dogs operated upon only 3 survived. He ascribes the mortality to hemorrhage, trauma, and anesthesia. He ligates both carotid arteries as a preliminary procedure, divides the superior longitudinal sinus, and arrives at the pineal by separating the cerebral hemispheres and elevating the splenium. The destruction of both carotid arteries and the superior longitudinal sinus seriously complicates the interpretation of results. Destruction of the great vein of Galen may also be an important complication. Into this vein passes practically all the blood from the interior of the brain. The collateral venous supply for the

vein is so inadequate that its occlusion results in an internal hydrocephalus. The amount of cerebral destruction incident to the above mentioned procedure of Sarteschi is also significant.

Evolution of the Operation upon the Pineal Body.

In a series of experiments on internal hydrocephalus by the author¹³ three years ago, the vein of Galen was occluded by the application of a silver clip, and in the development of this procedure a field of operation very close to the pineal was made accessible, and thus the possibility of removal of this structure was suggested.

By elaboration of the method of approach, an operation was devised which is free from the objections inherent to operations which entail cerebral destruction, vascular injury, or the endangering of the vitality of other cerebral structures. The results which might be noted could be attributed only to the uncomplicated loss of the pineal body. The operation to be described was successfully performed on young puppies from ten days to three weeks old under ether anesthesia plus a preliminary, relatively high dose of morphia. Despite the long duration of the operation, which usually required two and one-half to three and sometimes four hours, the animals recovered very quickly, and on the following day were almost as active and playful as the controls (Figs. 5 and 6).

An opening about 2 cm. in length was made in the vault of the skull, extending posteriorly to the inion and mesially to the midsagittal line. The dura was opened to and reflected over the superior longitudinal sinus. The occipital lobe was then carefully retracted and following the ligation of a small vein, which bridges the space between the brain and the falx cerebri, the tip of the tentorium cerebelli (osseum) was quickly exposed and the terminus of the vena Galena magna brought into view. Then a very tedious and painstaking liberation of this vein was begun. By alternately freeing the vein with careful blunt dissection and controlling the hemorrhage with pledgets of cotton, the inferior surface of the vein was liberated

¹³ Dandy, W. E., and Blackfan, K. D., Internal Hydrocephalus, an Experimental, Clinical and Pathological Study, *Jour. Am. Med. Assn.*, 1913, lxi, 2216; Internal Hydrocephalus, eine experimentelle, klinische und pathologische Untersuchung, *Beitr. z. klin. Chir.*, 1914, xciii, 392; An Experimental and Clinical Study of Internal Hydrocephalus, *Am. Jour. Dis. Child.*, 1914, viii, 406.

and the corpora quadrigemina exposed. The vein was then carefully elevated in order to work beneath it, and the median groove between the corpora quadrigemina was slowly followed anteriorly until the pineal body was reached. The pineal was then caught in a small biting forceps and removed. From a series of twelve dogs, of varying ages, not one survived the operation longer than one to two hours. Invariably the postmortem examination disclosed the ventricles full of blood, which was presumably the cause of death. The bleeding from the numerous venous and arterial radicles in the enveloping pia always resulted at the time of removal of the gland. Extirpation of the pineal necessitated opening the third ventricle because of the incorporation of this structure in its posterior wall.

Two years later the same plan of attack was again tried, but the pineal was dissected out more thoroughly before removal in order to minimize the hemorrhage when the ventricle was opened. Another addition to the technique of the operation and one which has proved of the greatest importance was to open the third ventricle at a point over the pineal body before attempting its removal. This not only permitted more room by release of the fluid, but, more important still, it collapsed the cerebral ventricles so that if hemorrhage should occur it would not be into the open ventricles and thus cause distention of the brain and possibly rupture of the cortex.

With these modifications this operative procedure became successful. The small amount of bleeding which resulted was sponged away with pledgets of cotton and was always under control.

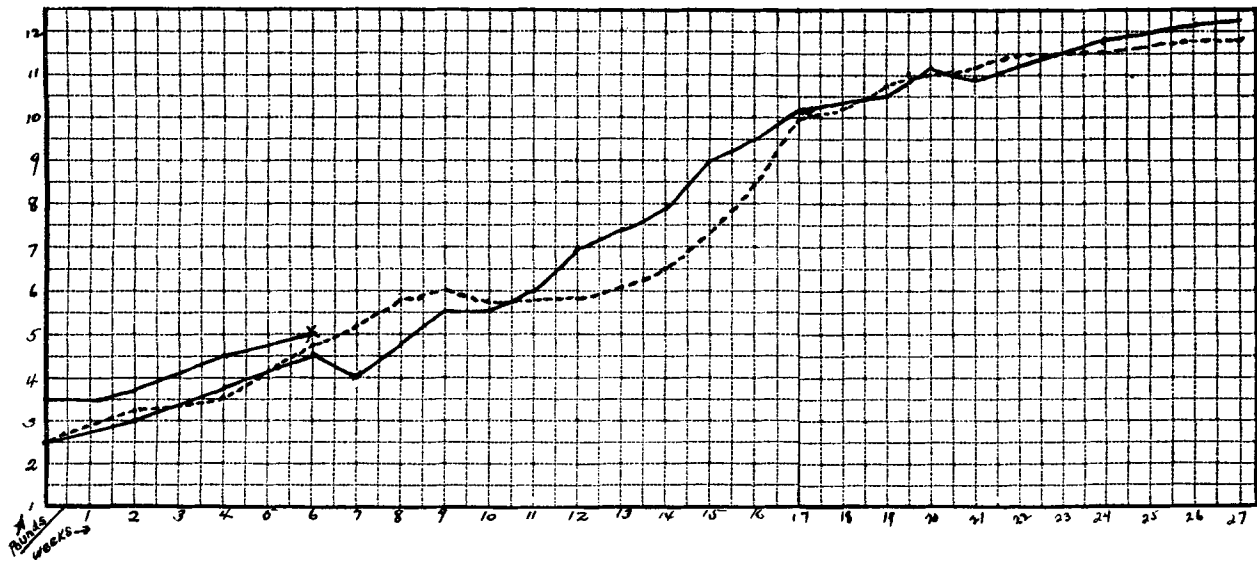
The operation as performed was, however, very unsatisfactory because of its great difficulty and the length of time required for its accomplishment. The most patient and assiduous care in the control of hemorrhage by wet and dry cotton pressure had to be exercised. It was necessary to hold the head quite motionless during this long and tedious procedure. With practice the pineal could usually be recognized because of its constant and dominant position at the junction of the median quadrigeminal groove and the third ventricle. However, very frequently, despite the greatest caution, the pineal would become covered with blood clot and unrecognizable and, perhaps, occasionally would be sponged away. When this was believed to have occurred an area of tissue from this accurately located

position was removed and examined microscopically. In all such cases a second piece of tissue was excised in order to insure complete removal of the gland. This, too, was studied with the microscope. In many instances the pineal area was further treated by an electric cauterizing needle. At times even with the greatest care, death resulted from bleeding into the ventricles. Successful complete extirpation resulted in only about 25 per cent of the cases operated upon in this manner.

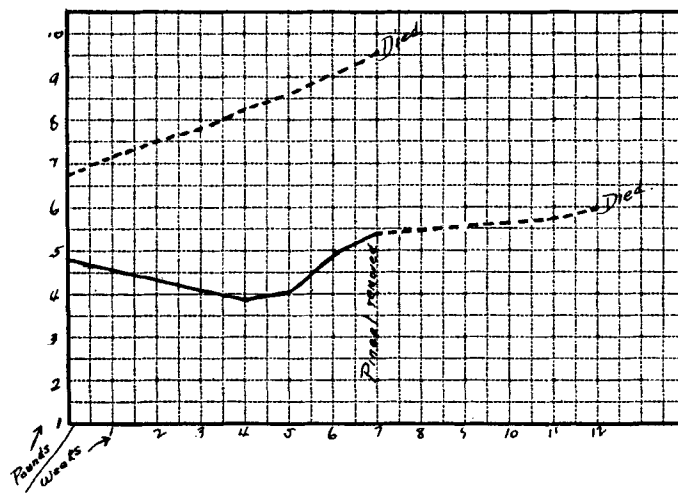
New Method of Pinealectomy.

The foregoing method was very capricious. To be of practical value the pineal body must be more easily reached and removed with greater certainty and less mortality. Consequently a new and simple method of attack has been evolved. Though more delicate and requiring more painstaking care, it can be done almost as easily as a canine hypophysectomy. The new operation can be done in less than one hour. It differs from the preceding operation in that the pineal is reached from in front through the third ventricle rather than from behind. In this way the extensive bleeding consequent to liberation of the vein of Galen is obviated, sidetracked as it were, and the operation can be performed almost bloodlessly. This is accomplished by dividing the splenium of the corpus callosum in the midline for a distance of about 2 cm. from its posterior terminus. This exposes the transparent roof of the third ventricle which is distended by the contained cerebrospinal fluid. A large anemic area is visible in the midline of the roof of the ventricle, between the two small veins of Galen. This is perforated and the opening enlarged backward to the origin of the vena Galena magna by releasing the blades of the forceps. The entire third ventricle is thus brought in full view and the pineal body is readily seen under the origin of this vein, in the median quadrigeminal groove. The pineal body can easily be grasped in the jaws of the cupped biting forceps and completely removed. The accompanying drawings By Mr. Broedel (Figs. 1 to 4) render any description of this operative procedure superfluous.

Practically no bleeding occurs during the exposure of the gland. A little bleeding follows its removal but this can easily be con-



TEXT-FIG. 1. Curve of weights of animals shown in Figs. 6 and 6 a. The base line represents the number of weeks and the abscissa the weight in pounds. The solid lines represent the weights of control dogs, and the broken line that of a pinealectomized dog, all being from the same litter.



TEXT-FIG. 2. A similar curve of two puppies from a litter 6 weeks old. The initial weights show a great difference. The broken line represents the pinealectomized dog, and the solid line the control. At the end of the 6th week the pineal was removed from the control dog, which had not developed normally. The removal of the pineal did not influence the growth.

trolled by a minute tampon of cotton. With collapsed ventricles the bleeding is outward through the wound and is therefore not to be feared. Not infrequently the aqueduct of Sylvius may be filled with blood. This has never caused any mortality because, before closure, the mould of clotted blood may be readily extracted, the aqueduct of Sylvius being in full view. To insure complete excision a second piece of tissue was invariably removed from the pineal region. With this method of operating there has been, as I have said, practically no mortality. It is, however, quite easy to become disoriented, even when following carefully the procedure which I am advocating. If bleeding and laceration of tissue are avoided, as they can be, and the midline is adhered to, there is little danger of losing one's bearings.

In every case a histological examination is made of all the tissue obtained at the operation (Fig. 7 b); and, after death, of the immediate region from which the pineal was removed.

Results Following Pinelectomy.

Our operations for extirpation of the pineal have been mainly upon young puppies, from 10 days to 3 weeks old. Of these one is living 15 months after the operation (Figs. 7 and 7 a); one died of distemper 1 year after operation (Fig. 8); several survived the pinelectomy 3 to 8 months. It is exceedingly difficult to raise puppies in the confined quarters of our laboratory. We were, however, unable to note any difference in the resistance of the operated and the control animals to the usual diseases.

When litters of puppies could be obtained, one or more of the animals were kept as controls. Little importance, however, should be attached to such comparisons because of the great variations found in members of the same family. The pineal was also removed in several adult male and female dogs, and three of these are living longer than four months after the operation (Fig. 9).

Somatic Development, Adiposity, and Mentality.

Careful observations have been made of the growth of the pineal-ectomized animals. Skiagraphs have been taken at various periods,

but there has been no evidence of either superior or inferior somatic development or adiposity (Text-figs. 1 and 2), save perhaps in a single instance. In this animal (Figs. 7 and 7 a) there was a slight increase in weight for a brief period about one year after the operation; this is disappearing, so that now it is scarcely noticeable. It might be attributable to overfeeding. There is nothing in the behavior of the pinealectomized animals to suggest mental precocity.

Sexual Precocity.

We have observed nothing to support the view that the pineal gland inhibits the sexual functions and that its removal is followed by excessive sexual development. Two bitches have lived for one year following the removal of the pineal; both were in heat ten months after the operation, or when about one year old. In neither animal has pregnancy resulted, and in neither was any abnormality observed in the generative organs.

The pinealectomized young male puppies observed for periods of from three to eight months, contrasted with members of the same litter, have given no evidence of sexual precocity or retardation.

Gross and Microscopic Study of the Glands of Internal Secretion.

Examination has been made of the various ductless glands which were obtained at autopsy. In none was a definite macro- or microscopic change observed. The tissues examined include the thymus, parathyroids, thyroid, hypophysis, adrenals, pancreas, liver, spleen, lymph glands, testes, ovaries, and mammary glands.

SUMMARY AND CONCLUSIONS.

1. Following the removal of the pineal I have observed no sexual precocity or indolence, no adiposity or emaciation, no somatic or mental precocity or retardation.
2. Our experiments seem to have yielded nothing to sustain the view that the pineal gland has an active endocrine function of importance either in the very young or adult dogs.
3. The pineal is apparently not essential to life and seems to have no influence upon the animal's well being.

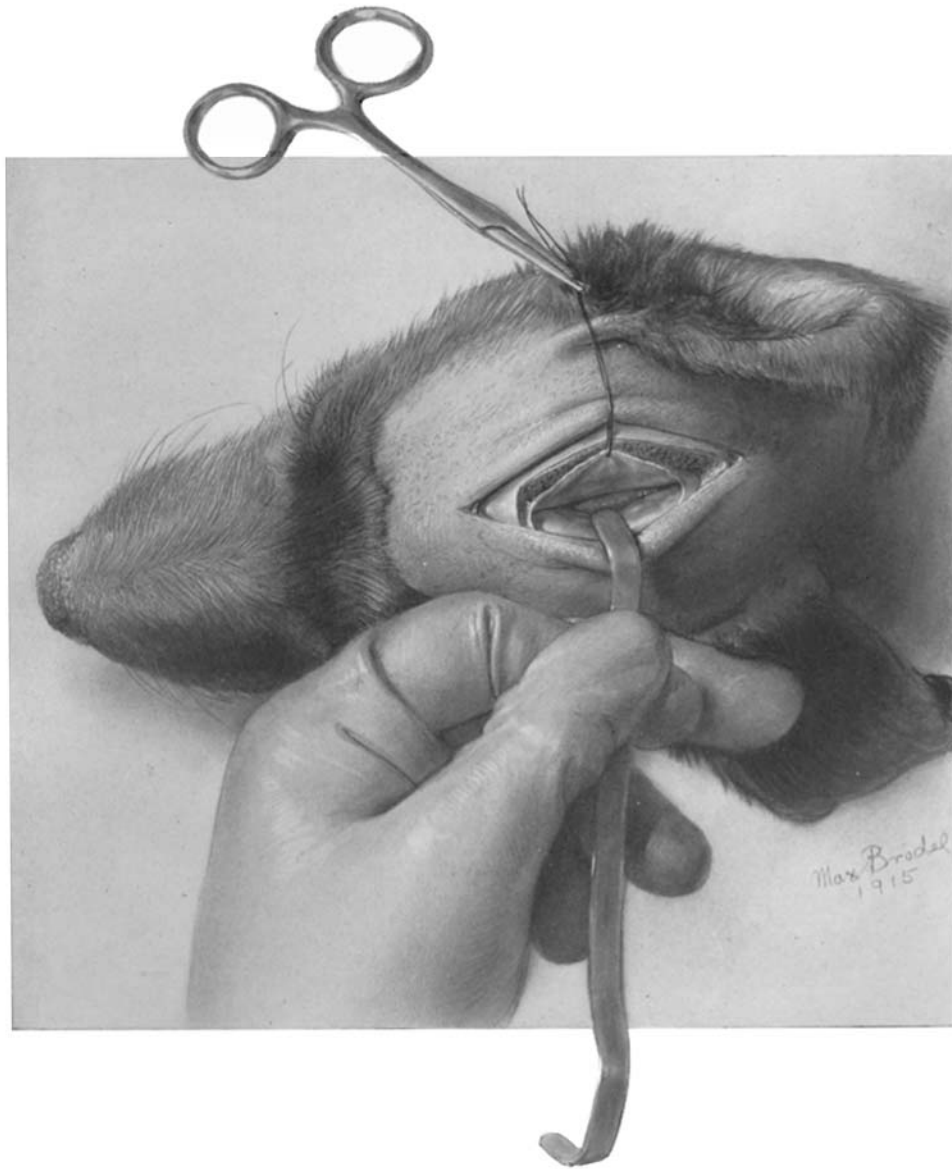


FIG. 1.

(Dandy: Pineal Body.)

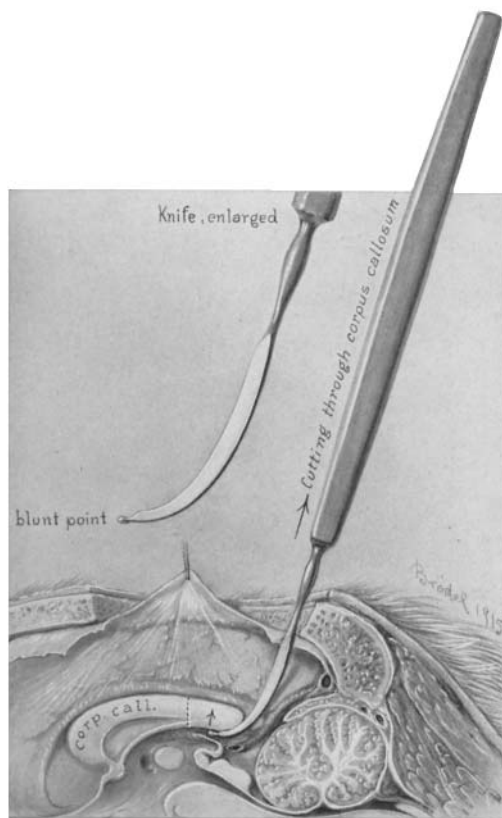


FIG. 2.

(Dandy: Pineal Body.)

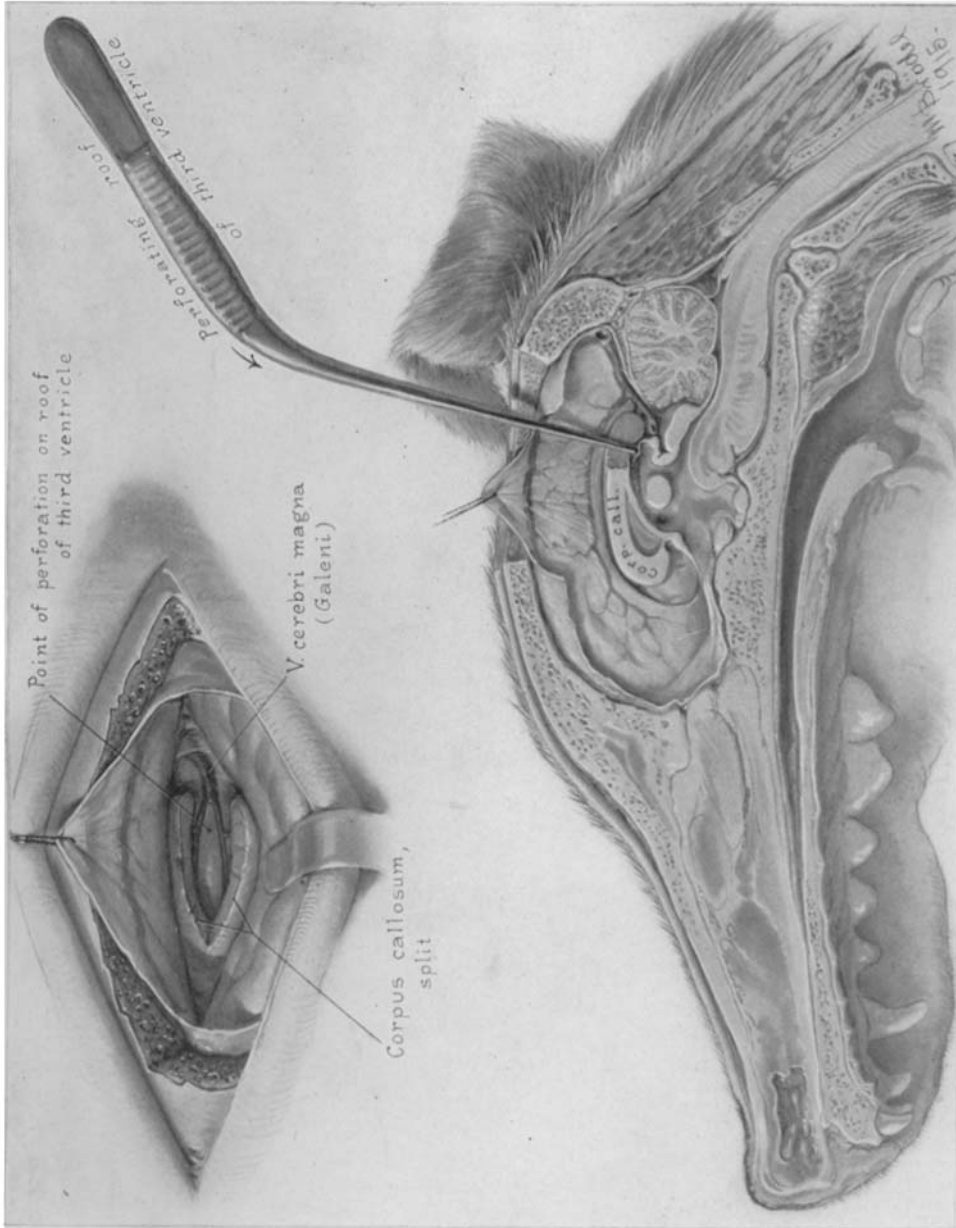


FIG. 3.

(Dandy: Pineal Body.)

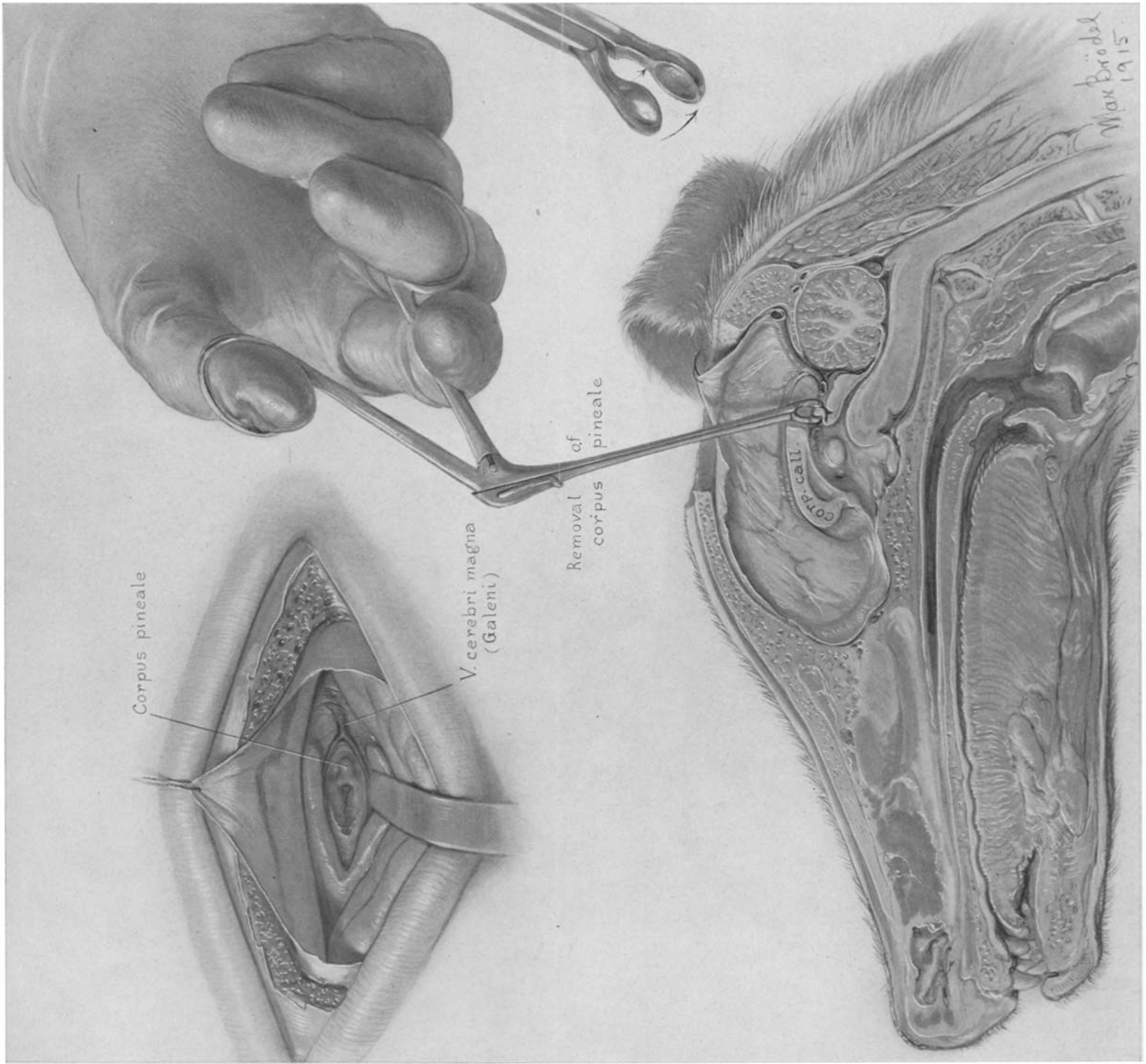


FIG. 4.

(Dandy: Pineal Body.)



FIG. 5.



FIG. 6.



FIG. 6a.

(Dandy: Pineal Body.)



FIG. 7.



FIG. 7a.

(Dandy: Pineal Body.)

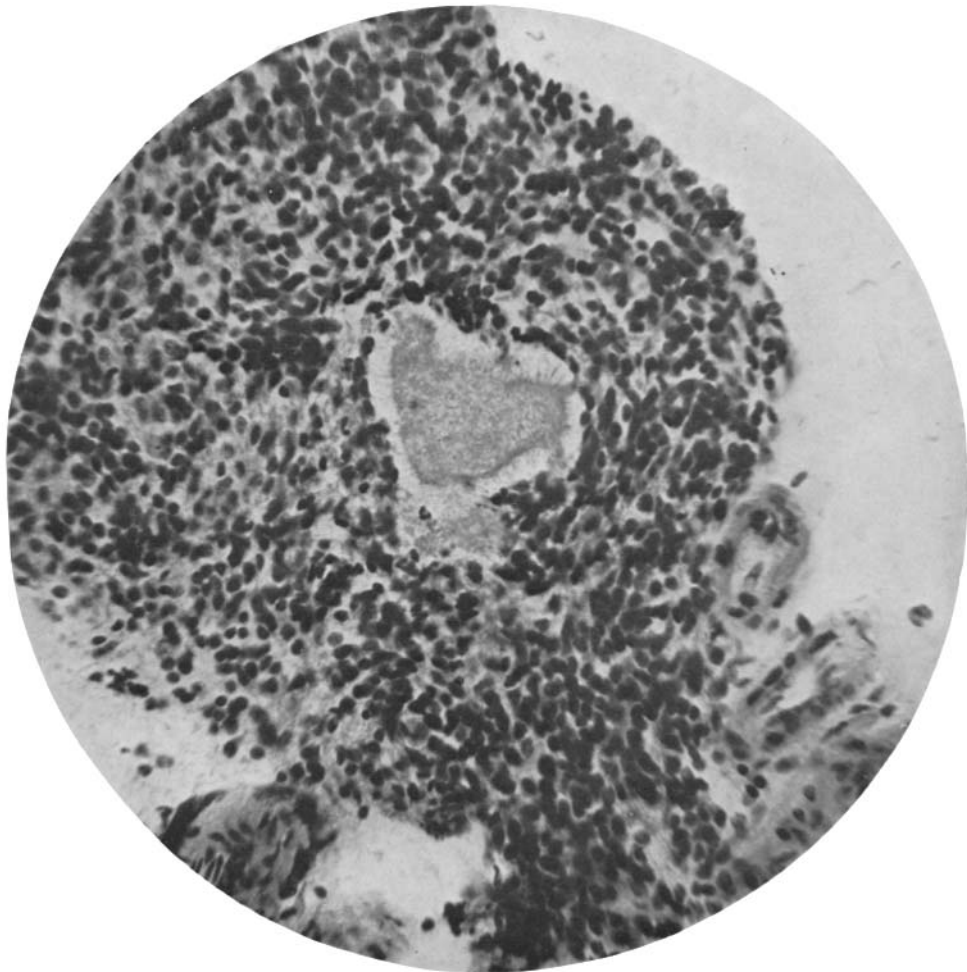


FIG. 7b.

(Dandy: Pineal Body.)



FIG. 8.



FIG. 9.

(Dandy: Pineal Body.)

It is a pleasure to express my gratitude to Professor Halsted for his interest and suggestions during the course of this investigation.

EXPLANATION OF PLATES.

PLATE 29.

FIG. 1. This demonstrates the location of the bony opening in the skull, the reflection of the dura over the midline, and retraction of the cerebrum, exposing the corpus callosum.

PLATE 30.

FIG. 2. This demonstrates the method of division of the splenium.

PLATE 31.

FIG. 3. The upper plate (enlarged) demonstrates the splenium divided, exposing the roof of the third ventricle with its *venæ Galenæ parvæ*. The lower plate shows the method of perforation of the roof between these veins.

PLATE 32.

FIG. 4. After opening and widening the defect in the roof of the third ventricle, the pineal is well exposed, as shown in the upper plate, and is easily grasped by the biting forceps, as shown in the lower plate. The jaws of the biting forceps are also shown separately.

PLATE 33.

FIG. 5. Puppies 14 days old. The photograph was taken 24 hours after removal of the pineal. The absence of any operative or glandular effects is well shown.

FIG. 6. Litter of 5 puppies, 3 of which have had the pineal removed and 2 of which are controls. The operated animals are recognized by the shaved heads. Photograph taken 2 weeks after operation.

FIG. 6 a. Pinelectomized animal (black), 4 months after operation, the operation being performed when the dog was 3 weeks old. The white dog is a control. The comparative weights of the animals are shown in Text-fig. 1.

PLATE 34.

FIG. 7. Pinelectomized female dog, 4 months after operation.

FIG. 7 a. The same animal, 14 months after operation. This is the only pinelectomized animal showing any adiposity. This has since disappeared.

PLATE 35.

FIG. 7 b. Photomicrograph of pineal removed from the dog shown in Figs. 7 and 7 a.

PLATE 36.

FIG. 8. Dog in which the pineal had been removed 6 months previously, when the animal was 18 days old.

FIG. 9. This demonstrates the staring expression which occasionally results from injury to the corpora quadrigemina during removal of the pineal.