1946

Pineal body

Dale Caldwell Hathaway
University of Nebraska Medical Center

THE PINEAL BODY

Dale C. Hathaway

Senior Thesis Presented to the College
of Medicine, University
of Nebraska, Omaha,
1946

TABLE OF CONTENTS

INTRODUCTION

Although this small, midline structure has been known to anatomists and the medical profession since the time of Galen (A. D. 131-201) at least, and possibly before, there is still a mystery concerning it. Its purpose, its function, its origin as one of the few midline structures of the adult human body have all been speculated on through the years, but still nothing definite is known about the pineal body. Great steps have been taken in several major fields concerning this little, yet important (?) gland in recent years. It is the purpose of this thesis to briefly review, digest, and summarize the advancements made upon this organ as found in the literature of the past three decades.

Also, I might add, it is the result of a desire of mine first brought to my attention in my Junior year of medicine by one of my medical instructors, who covered this subject of the pineal body with the words--"little is known about the pineal gland"--and issued at the same time with startling clarity a challenge to find out more about the gland, which is briefly covered in most medical books by a few sentences. I have found since then that although it may be true that little is known at the present time about the pineal gland, if it is a gland, that there may be a period in the relative near future when the medical profession will realize that the pineal body may have more to do with the human structure than was formerly thought possible.

HISTORY

The existence of the pineal body was known to the Greeks and Romans. It was first known as κωνάριον or conarium, meaning pine cone, from its conical shape. It was also called turbo (a whorl), glandula turbinata, and scolecoid (worm-like). The latter name was commonly used by Galen, who did much of his dissections on oxen, sheep, and apes. He mentioned in his writings, however, that other men called it the epiphysis. He, too, had stressed its relationship to the great vein of the brain which bears his name today. Various ideas as to its function were put forward, typical of which was the notion that it acted as a valve, regulating the quantity of spirit (cerebrospinal fluid) necessary for the psychological requirements of the individual. The Romans were among the first to consider it a gland and, therefore, described it as the glandula pinealis (pine cone). During the next few centuries little advancement was noted concerning the pineal body, except that its name was changed to penis cerebri, virga cerebri, epiphysis cerebri, and glandula superior, the latter to correspond with the hypophysis or glandula inferior.[55] The situation seemed to be clarified somewhat in 1664 when Thomas Willis described it as pinealis or penis, and the name has been used to this day.

As one may have noticed by the use of so many varied names, the functions of the pineal body has caused much speculation. As these speculations are of interest when considered in the history of the pineal body, they will be discussed to some length. Galen thought of the pineal body as a secreting gland, and later men considered it as a control of the cerebrospinal fluid. The belief that the pineal body was in some way connected with the circulation of the cerebrospinal fluid, which was first described by Thomas Willis in 1664 had a very long life. William Cowper described in 1698 the pineal body as being a lymphatic gland and capable of-"receiving lympha from the lymphe-ducts which pass the third ventricle of the brain to the infundibulum and pituitaria glandula".(55) This was a commonly held fact as late as the middle of the nineteenth century, e.g. Magendie and Jacob Henle. However, with our modern microscopes and histological technique it is easily demonstrable that the pineal body isn't a lymphatic structure.

It is a curious fact that in 1662 René Descartes, a philosopher of sorts, wrote a treatise on the function of the pineal body. He regarded the human body as an earthly machine presided over by the "rational soul" which occupied the pineal gland-"the little gland in the middle of the substance of the brain".(25) According to Descartes, the pineal received the animal spirits from the arteries, stored them up, and passed them on to the cerebral ventricles-a second reservoir-whence they were transmitted through the hollow nerves over the body. When the spirits in the ventricles were uncertain about their proper destination, the pineal directed them by leaning to one side or another of the middle line. Other authors held similar views, but placed the seat of the soul in pituitary, liver, and heart as these were single or unpaired organs of the body. None of these statements were widely accepted, due to the obvious lack of proof. However, it is important to note that modern theosophists believe that in the later perfection of the human race the pineal body will accommodate the seventh sense-the power of divine insight-while the sixth sense, that of comprehending unvoiced thought or of psychic receptivity, is placed in the pituitary.

The work on the pineal region in the latter part of the nineteenth century and the commencement of the twentieth century was attended by a marked advance in our knowledge of the true nature of the pineal apparatus in all its aspects-geological, zoological, embryological, and phylogenetical. It is to this period that we owe the conception of the vestigial nature of the pineal body-a non-functioning, median, third eye. Leydig in 1872 found the parietal organ in the embryos of lizards of the suborder of Lacertilia. In 1875 Goette described the epiphysis in another order of Vertebrata. It was described in higher forms of vertebrates by other authors at about this time, some of whom disputed Goette's works. Rabl-Ruckhard in 1886 suggested the function of the pineal body was to estimate the heat of the sun's rays-in other words, it acted as a thermal sense-organ rather than a visual one, but this was later disproven by Nowikoff in 1910. His experiments, however, raised much interest in the presence of pigment in and about the pineal organ, particularly, in reference to (1) the origin of light perceiving organs in general and (2) the occurrence of regressive changes and melanotic tumors in the human pineal organ.[25]

In the past three decades, interest in the pineal body has been revived, especially in connection with its supposed endocrine function and a surgical approach to pineal tumors. The former aspect has particularly led to a more exact study of its histological structure and of experimental work on animals along the lines of extirpation, feeding with whole or desiccated preparations of the gland, injection of extracts, and grafts as shown in the works of Anderson and Wolf,[2] McCord,[46] Engel,[16] Rowntree,[57] Davis,[13] and Globus and Silbert.[27]

ANATOMY
Embryology and Histology

Before further considering the other aspects of such a structure as the pineal body, it will be profitable to review the anatomy, embryology, and histology of this very interesting part of the brain. It is only by doing so that we can hope to interpret signs and symptoms, the physiological aspects, and the different, various histological pictures that are met with in tumors of the pineal body and call for surgical intervention.

The pineal body, as mentioned before, has been known since the days of ancient Greeks. It resembles a minute pinecone and springs from the posterior part of the roof of the third ventricle. The human pineal is small, oval, and red in color. Its average dimensions are:-Saggital 8.4 mm., frontal 6.3 mm., from above down 4.2 mm. It is a little smaller in the female than in the male and proportionally larger in the child than in the adult.[60]

Its base is connected on each side by a short peduncle with the habenular commissure. It lies in a depression between the superior corpora quadrigemina, which form its relations inferiorly. Above, the pineal body comes into contact with the velum interpositum and the splenium of the corpus callosum. The apex is quite free and is directed downwards and backwards, while the base is directed in the opposite direction. The base of the pineal is a part of the posterior boundary of the cavity of the third ventricle. The pineal is partially covered by pia mater, which is derived from the lower layer of the tela choroidea or velum interpositum. The anterior third of the pineal is covered by the layer of ependyma which forms the floor of the dorsal diverticulum or suprapineal recess. This is continuous with the ependyma lining the cavity of the third ventricle and is reflected anteriorly over the superior commissure and into the pineal recess.[(24) (9)]

The roof of the superior pineal recess is continuous with that of the third ventricle and has numerous choroidal villi, hanging downwards from it and resting on the upper surface of the pineal body. The posterior two-thirds of the pineal body is covered by the lower layer of the tela choroidea which is firmly adherent to its capsule. The pineal is in close relationship with the great cerebral vein, which separates it from the corpus callosum and commissural fibers of the fornix. The splenium projects backward beyond the apex of the pineal body.

The lower surface of the pineal is separated from the groove between the superior colliculi by a fold of pia mater, which forms a recess known as the subpineal cul de sac of Reichert.[9] This may reach forward as far as the posterior commissure or may become obliterated by adhesions. The lateral surfaces are also covered with pia mater which may be continued backward from the sides and apex of the gland as a fold, which contains between its layers, vessels, nerves, and the ganglion conari. The nerve fibers are described as belonging to the sympathetic nervous system and as being of two kinds (1) fine, which are more numerous, and (2) coarse.

As mentioned before, the base is connected by peduncles, superior and inferior, and an intermediate or lateral peduncle, which connects the pineal body with the medial surface of the thalamus. The superior peduncle contains medullated nerve fibers belonging to the superior or habenular commissure. It is continued forward on each side as the habenula. The inferior peduncle carries similar fibers of the posterior commissure. Lying between the two commissures is the pineal recess. In spite of the posterior commissure being a familiar and valuable landmark, it has been difficult to trace its connections with certainty. Many men are of the opinion that some of the fibers arise in the nucleus of origin of the median longitudinal fasciculus and that the decussating fibers have connections by way of this tract with nerve fibers of the eye muscles. It may also contain fibers which originate or end in nuclei situated in the tectum opticum.[24]

Examination of the structures which lie around the pineal area and are liable to be compressed by a tumor in this area is of much importance, especially, in view of future aspects of this thesis. A transverse section of the brain in this area would show the fornix with its fimbrial lying slightly to both sides and superior to the pineal body. The fornix is shown to be connected to the body of the corpus callosum. Overlapping the fimbria of the fornix on each side is the choroid plexus, which projects into the lateral ventricle. The size, vascularity, and density of the plexus varies considerably in different individuals. On either side of the pineal body is the pulvinar of the optic thalamus. This is separated from the pineal body, superior colliculus, and superior brachium by pia mater containing blood vessels. Lateral to the pulvinar is the internal capsule, passing between the caudate and lenticular nuclei and coursing downward into the crura cerebri. Immediately beneath the pineal body is the roof of the aqueduct, containing the tectospinal and tecto-bulbar nuclei. Around the aqueduct is the central gray matter, and below it, the various nuclei of the third nerve, the nuclei of the fourth nerve, and the medial longitudinal fasciculi, which if traced down-wards are found to be connected on each side with the superior olive, the nucleus of the sixth cranial nerve, and that of the vestibular nerve. Ventral to the nuclei of the third nerve are the red nuclei, the decussation of the rubrospinal tract, and the substantia nigra; while dorso-lateral to the red nucleus is the medial lemniscus.

Ventral to the red nuclei is the substantia nigra, and near the outer borders of this are seen the medial geniculate bodies. Passing upwards round the outer side of the crus cerebri are the posterior cerebral and superior cerebellar arteries, with the fourth nerve running ventrally and forwards between them. The basal vein occupies the recess between the crus cerebri and medial geniculate body on the inner side, and the tail of the caudate nucleus, inferior horn of the lateral ventricle, choroidal fissure, fimbria, and hippocampus are on the outer side.[9]

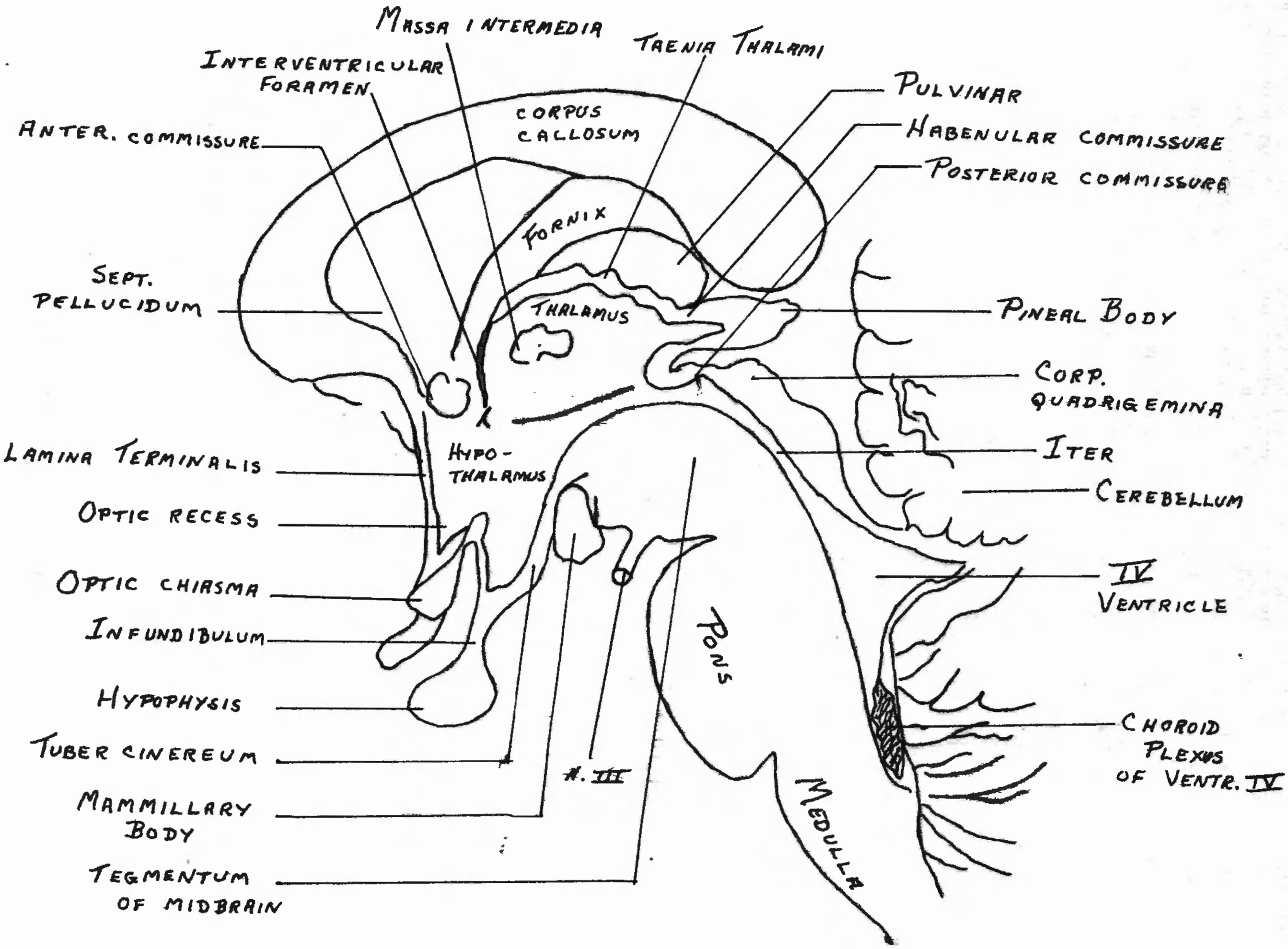

Fig. 1 Median Saggittal Section of Brain Stem. Strong-Elwyn[62]

In a medial section, the apex of the pineal body is seen in close relationship to the superior vermis of the cerebellum. Should the pineal enlarge, it may exert direct pressure on this and the superior peduncles or brachia conjunctivae. A pineal tumor, enlarging forward into the third ventricle, would exert pressure on the interpeduncular, subthalamic regions, and the optic thalami laterally.(67)

Embryologically speaking, one of the first indications of the development of the pineal system in man is the thickening of the ependyma in the posterior part of the roof of the diencephalon and the adjacent parts of the alar laminal as seen in a 15 mm. embryo. This thickening has the form of a longitudinal band which is slightly raised above the general surface and is grooved on its under surface. It lies in front of the posterior commissure, which has already appeared. Soon, by a forward growth of the anterior end of the thickened band and a deepening of the groove, the rudiment assumes the typical form of a primary diverticulum.

In a 20 mm. human embryo, the walls of the diverticulum show a division into the three typical zones of the neural tube, namely, an inner thick ependymal layer, a thin middle layer or nuclear zone, and an outer reticular or marginal zone. The inner ends of the ependymal cells which immediately surround the lumen are clear and destitute of nuclei. They show a radial arrangement and are bounded by an internal membrane. The outer zone is limited by a less definite external membrane and is closely related to large endothelium-lined spaces and capillary vessels.

In a 22 mm. human embryo, the simple primary diverticulum is subdivided by a transverse fold into a hollow, bilobed anterior segment, and a single median posterior segment. The habenular commissure has also appeared, and two diverticula from the dorsal sac have begun to grow backward on either side of the main pineal diverticulum. In a 6 cm. human embryo, the anterior stalk has increased in size and a secondary pineal stalk has developed. This forms a little more than half of the total outgrowth, the distal end of which consists of the main pineal diverticulum and a smaller posterior diverticulum, which lies immediately above the posterior commissure. The anterior lobe consists of a number of irregularly branched processes of epithelium, which grow into the vascular mesenchyme in front of the main diverticulum of the pineal body and above the habenular commissure. Similar proliferating outgrowths of ependymal cells from the sides of the main diverticulum are seen to invade the mantle zone, but these lie beneath the external limiting membrane and have not yet come into contact with the blood vessels of the surrounding mesenchyme. Two diverticula are seen in front of the pineal body. The more posterior of these representing the future suprapineal recess, and the anterior one probably being a rudiment of the paraphysis. This infrapineal recess corresponding to the posterior pineal diverticulum, mentioned above in the preceding specimen, disappears at a later stage of development—probably by opening out into the cavity of the third ventricle. The central cavity of the body of the main pineal diverticulum, which according to Krabbe[40] becomes closed by constriction at the neck, persists for a variable time.

In a four and one half month fetus, cut in a coronal section, the anterior lobe is seen to be partially separated from the main part of the organ by two fibro-vascular septa, which pass obliquely downwards and medially toward the center of the pineal body, traversing about one-third of its total width. The remaining median third corresponds to a zone where the anterior lobe is continuous with the substance of the main posterior lobe. The structure of the two lobes is similar, but the center of the anterior lobe is more homogenous. Each lobe consists of a lobulated mass of small epithelial cells with deeply stained oval nuclei. The most active growth is at the periphery, where irregularly branched epithelial processes are reaching out into the surrounding vascular connective tissue. The epithelial cells are derived from the inner ependymal zone of the diverticulum, but there are also a number of cells that are nearer those of the mantle zone, being vesicular and pale as contrasted by their position and deeply stained nuclei of the undifferentiated ependymal cells. At the surface branched club-shaped processes intermingle with vascular processes, which appear to grow inward between the epithelial cords. The deeply stained cells surrounding the clear vascular areas have the appearance of epithelial cords cut in various directions or "rosettes".(25) This illusion is due to the oval, deeply stained nuclei arranged radially around a small, palely stained central zone, which is formed by the inner ends of the cells coming into contact in the central axis of the cord. This arrangement of alternating series of branched epithelial and vascular cords is the key to the mosaic appearance, described by Globus and Silbert,(27) as characteristic of the later stages of fetal and early postnatal life.

At the end of the fifth month, there is an increase in the number of cells and blood vessels in the human fetus. The diverticulum becomes still narrower, and the entire pineal anlage measures about 2 mm. The pineal recess is now closed, forming a cavity instead of a diverticulum. The anterior and posterior anlagen are completely fused. The pineal body now presents the histological features of a primitive glandular structure. At the rostral end of the bud, several large tubules form a vanguard of a large aggregation of smaller tubules. The former are wide open, irregularly branched, and are lined by columnar epithelium, while the latter are lined by cuboidal cells.

In the fetus of seven months, the so-called clear areas show an increase in the number and size of the cells in the clearer zones, and the vessels, prominent in an earlier stage, are somewhat less conspicuous, being displaced to the periphery of this zone. In the eight and one-half fetal pineal body, another phase becomes apparent. The pattern, typifying the structure of the gland during late prenatal and early postnatal life, is now seen. Streams of small round cells, poor in cytoplasm and deep staining nuclei, break up the pineal region into irregular squares, which are populated by cell masses of lesser density and of less intense staining qualities. The latter are easily distinguished from the small dark cells in the encircling streams by their lighter appearance and by their larger size.[27]

The last days of fetal life and first few days of postnatal life are marked by further striking alterations in the histology of the pineal body. The characteristic pattern of clear areas surrounded by narrow zones of deeply staining cellular elements becomes more apparent. At the periphery may be seen large, distended blood channels, giving the appearance of massive hemorrhages. These large vessels are similar to the picture seen in the development of a gland of internal secretion--suprarenal (Aschoff [1]). Thus, a similarity in evolutional features between an organ of internal secretion and a structure of unestablished physiological activity is indicated.

At the end of the third week in postnatal development of the pineal body, the pattern, mentioned above, reaches its highest stage of development. There is an increase in size of the large cells with an associated increase of vascularity, but there is no apparent diminution in the number of small darker cells. The increased vascularity of the large cells is another feature suggestive of glandular function. From the fourth week of postnatal life to the ninth week there is no further striking changes seen. Around the ninth week, the structure begins to lose its mosaic character as the small cells begin to break up their continuity and to decrease in number. At the fourth to fifth month this change is pronounced, there being only small islands of small dark cells left. These cells have assumed a new character, becoming elongated and resembling fibroblasts. At the end of the ninth month little is left of the old mosaic structure.

From the ninth to the eighteenth month the pattern gradually changes to that characteristic of the transition between the infant and adult form. There is now a beginning alveolar arrangement of cells and the appearance of connective tissue trabeculae. This is more apparent at the end of twenty-three months. Also, noticed at this stage were groups of basophilic granular cells and occasional eosinophilic granular cells, indicating that mesodermal components contribute to the organization of the pineal body.[27]

From now on the architectural changes are not readily distinguishable over long periods. At five and a half to seven years the pineal structure approaches that of the mature gland. It is believed that the pineal body increases in size until about seven years of age. At this time involution is said to begin and to continue to fourteen years of age. This is manifested by an increase in the amount of neuroglia and by the development of hyaline changes in both the septa and the lobules. The so-called "brain-sand granules" (corpora arenocea) also begin to appear. These are laminated structures consisting mainly of phosphates and carbonates of calcium and mangesium.[49]

In the adult organ, there is said to be three types of cells: (1) what appear to be nerve cells provided with tuberous appendixes and processes ending in bulbs, (2) pineal cells proper or specific parenchymatous cells without appendixes and possessing some structural characteristics interpreted as secretory, and (3) cells with fibrillary expansions, apparently neuroglia. The investigations of Hortega[14] have shown conclusively that the lobules of the pineal body are composed solely of two categories of cells, the parenchymatous and the neuroglia cells. In effect, that leaves the cells of types (1) and (2) above as merely two aspects of a single parenchymatous cell type. The parenchymal cell, it is universally agreed, is developed from the pineal enlage and is of nervous origin. The histogensis of the small cell is disputed. Horrax and Bailey(34) regarded the small cell as a glial cell of neuroectodermal origin which developed with the large cell in the pineal enlage. Globus and Silbert(27) consider the small cell of mesenchymal origin with a transformation to fibroblasts in the older pineal bodies.

Because the tumors classified as pinealoma characteristically contain the two types of cells observed in pineal tissue at the time of birth, it is concluded that their cells are likewise of neuroectodermal origin. Pinealoma, therefore, is merely another type of glioma representing neoplastic pineal tissue at its highest stage of development-at about the time of birth.

The blood supply of the pineal gland, according to Gray,(28) is as follows: (1) Arteries-the immediate arterial blood supply arises from several branches of the superior cerebellar artery, which arises near the termination of the basilar artery. It passes lateralward, immediately below the oculomotor nerve, which separates it from the posterior cerebral artery, and then winds around the cerebral peduncle to arrive at the upper surface of the cerebellum, where it divides into branches, (2) Veins-the basal vein is formed at the anterior perforated substance by the union of a small anterior cerebral vein, the deep middle cerebral vein, and the inferior striate veins. This vein passes backward around the cerebral peduncle and ends in the internal cerebral veins (veins of Galen). These latter veins drain the deep parts of the cerebral hemispheres and unite after a short distance to form a short trunk, the great cerebral vein (great vein of Galen) which is a short median trunk that curves backward and upward around the splenium of the corpus callosum to end in the anterior extremity of the straight sinus. Clark[7] has described a formation of arachnoid in relation to the floor of the straight sinus where the great vein of Galen opens into it. This structure somewhat resembles a large arachnoid granulation of the usual type, but its stroma consists of dense pial tissue containing a sinusoidal plexus of blood vessels and several large blood sinuses. It has been termed the suprapineal arachnoid body. Clark[7] has suggested that this body may provide a ball-valve mechanism whereby the venous return from the great vein of Galen is regulated and controlled.

The nervous supply of the pineal body is difficult to ascertain. The existence of typical nerve cells, showing both Nissl granules and axis cylinder process as a normal constituent of the human pineal organ has been not only doubted but denied by some recent workers, who regard the occasional occurrence of such cells as anomalous. There appears to be transitional stages between nerve cells and typical parenchyma cells; this, probably, in some cases of branched pineal cells with bulbous extremities (del Rio Hortega)[(14)] causes the cells to be mistaken for fully developed nerve cells. True nerve cells, apparently belonging to the sympathetic system, are occasionally seen on or near the surface of the gland or in close relationship with the vessels contained in the trabeculae. The question of whether the parenchyma cells themselves are sensory in nature and capable of transmitting a sensory impulse from an afferent pineal nerve to an efferent pineal nerve is one of practical interest. Should they possess this function, their anatomical connections fully warrant the assumption that a reflex mechanism may exist within the pineal organ, which is capable of being influenced by impulses reaching it through its afferent nerve-fibers and transmitting such impulses by efferent fibers to the organs or regions to which these nerves are distributed.

An anatomical basis for this hypothesis has been suggested in the works of Pastori[52] and Clark[7] on the nervous connection of the epiphysis. Pastori demonstrated in the human subject the constant presence of a sympathetic ganglion situated in the membranes just behind the posterior pole of the epiphysis. This ganglion is connected by a large number of very fine nerve fibers with the epiphysis and by other coarser nerve fibers, which form a definite bundle which joins the plexus of nerve fibers on the great cerebral vein of Galen and its tributaries. This bundle is the nervus conari of Kolmer. Clark in his studies found the nervus conari emerging from the tip of the gland and running an uninterrupted, unbranched course to reach the dura mater of the tentorium cerebelli; traveling in the floor of the straight sinus. Clark also found the nerve traveling through the suprapineal arachnoid body, described by him. Thus, it appears possible that some of the fibers may be efferent nerves from the ganglion to the gland, and others afferent from the gland to the plexus of nerve fibers on the neighboring vessels and arachnoid bodies, thus furnishing a means by which the epiphysis may be influenced by or act upon the sympathetic system.

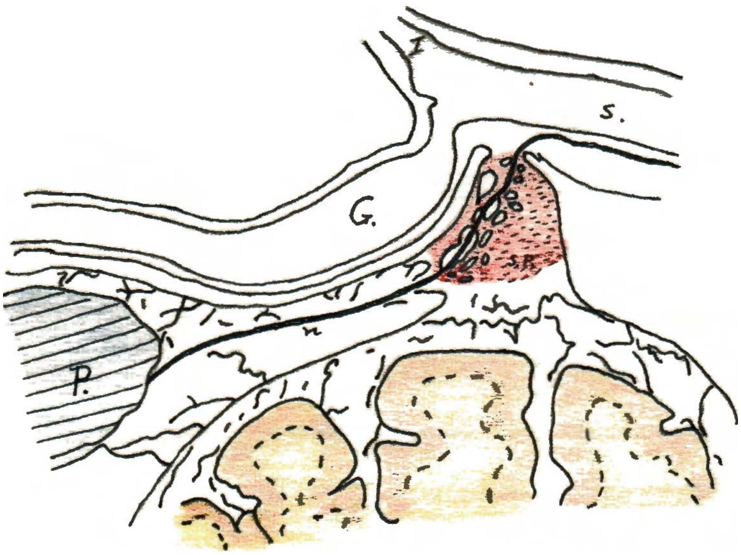

Fig. 2 Course of the Nervous Conari in Human Brain. Clark(7)
G-Great vein of Galen; I-Inferior sagittal sinus; n-nervus conari; P-Pineal body; S-straight sinus; s. p.-suprapineal arachnoid body

ENDOCRINOLOGY and PHYSIOLOGY

Outside of certain Australian lizards in which the pineal gland has become highly specialized as a centrally placed rudimentary third eye, the function of the pineal gland has not yet clearly been defined. As a result of clinical observations, Marburg in 1907 formulated the idea that the pineal body during childhood inhibits both sexual and somatic growth, and that when this gland is destroyed by tumors, growth (sexual, somatic, or both) begins earlier and continues uncontrolled. Various authors have since endeavored to prove such a relationship, but the results obtained are of a conflicting nature and the question still remains unsolved.

Modern experimental efforts to elucidate the function of this body have consisted of:

Pinealectomy-A survey of the results of extirpation of the pineal shows that about half of the authors obtained premature development of the sex organs, more often in the male than in the female, frequently accompanied by increased body growth, while the remaining workers obtained negative results. A critical review of the methods of data shows that all of the work is open to criticism on at least two points: (1) the normal range of the age of puberty and rate of growth of the particular breed under the specific laboratory conditions of the experiment has not been studied, (2) the necessity has not been recognized of using enough animals under standardized conditions of strain, age of operation, diet, and age of death to allow statistical analysis of results. This is difficult due to the high mortality of the operation. Andersen and Wolf,[2] in 1933 and using rats under controls eliminating many of the previous conditions just mentioned removed the pineal body and came to the conclusion that neither the rate of growth, age of puberty, nor weight of the pituitary, thyroid, adrenal, nor thymus is affected in either sex. They could find no difference in weight of the testes in males or the occurrence of normal oestrous cycles in females. Sullens and Overhouse[63] in 1941 came to the same conclusion.

Feeding Experiments-McCord[46] has reported the feeding of fresh pineal glands to four hundred young animals who developed, he claimed, early precocity and adiposity. Hoskins, on the other hand, found such feeding experiments of no value, and no changes taking place.

Pineal Implants-In implantation of pineal glands, Kozelka showed negative results in chicks, but Dubowik found an increase in rate of growth in rabbits. Lahr has shown some retardation in the gonadal development in both male and female, but most influence upon the body growth. In 1936 Fleischmann and Goldhammer(18) claimed to be able to arrest regular oestrus in rodents through the implantation of the epiphyses of infantile animals. Examination of their work shows that t he period of arrest varied from four to six weeks, after which time the regular cycle reappeared. Tarkhan in 1937 repeated their work exactly and received negative results. Abd-el-Malek(48) in 1939 repeated similar experiments only using infantile epiphyses in rats of the same species, where as Fleischmann and Goldhammer used rat epiphyses in female mice. Abd-el-Malek received negative results in his experiment.

Injection of Pineal Extract-No definite results of pineal extract injections had been demonstrated until Engel(16) appeared to have found an antagonism of the pineal extract toward the growth hormone of the anterior lobe of the pituitary as well as toward those pituitary hormones affecting luteinization and maturation of the ovarian follicles. On repeating the same experiments in the rat and rabbit, Fleishmann and Goldhammer(18) found that injection of epiphyseal extract as well as subcutaneous implantation has no effect on the action of gonadotropic hormones. Paul Engel[16] in 1939 confirmed the works of Fischer,[17] who found the vaginal membranes of infantile female mice were inhibited from opening by use of pure pineal extract. By using a less pure extract, these men advanced the opening of the vaginal membranes. The differences in results of other investigators brings up the possibility of two hormones in the pineal gland.

In view of all the confusion, Rowntree and his coworkers[58] introduced a new factor in the injection experiments. They tested the effect of pineal gland extract not only on the individual animals receiving the injections intraperitoneally, but also on the offspring of successive generations of parent rats. At the time of their report, five generations of pineal strain of rats had been under observation. In the first generation, no effect was apparent other than moderate loss of weight and excess sex excitation and early breeding. In the second generation definite retardation of growth with mild precocity of gonadal development occured. In the third to fifth generations, changes along the same lines but much more greatly evident were seen, both in the retardation of growth and in the acceleration of gonadal and bodily development, leading to the term "precocious dwarfism". The dwarf stature of these animals is permanent, and though small in size, they show an acceleration in the opening of their ears, the eruption of their teeth, the appearance of fur, the opening of their eyes, the descent of their testes, or the opening of the vagina. The average rat of the fifth generation under pineal treatment was described as less than one-half the normal size with both bodily and gonadal development occurring precociously. The animals, however, are physically weak, irritable, and nervous. The extract used was from beef glands of average killing age. Continuing his studies, Rowntree[57] in 1936 came to the conclusion that the rate of growth is accelerated by the thymus and retarded by the pineal gland, while the rate of development is accelerated by both glands.

Aronstam[3] has used a pineal substance clinically for organic and psychic impotence. He hasn't drawn any conclusive opinion as yet, but has said the results were encouraging.

Wade[66] in 1937, using fresh beef pineal extract, failed to note any antigonadotropic activity in infantile female rats nor any estrogenic activity in adult spayed rats, thus giving a synergistic effect to pineal extracts.

PATHOLOGY

The various pathological conditions which arise in and around the pineal gland may be discussed in relation to the actual lesion itself, in relation to the local changes produced inside the cranium, and in relation to the somewhat vaiable general skeletal and endocrine changes which are sometimes associated with such pathological conditions.

The pineal body has been known to undergo simple hypertrophy, atrophy, and to be associated with other pathological conditions, such as myxedema and polyglandular dysfunctions. The other pathological conditions arising in and about the region of the pineal may be classified as follows: (1) Teratomas, (2) Pinealomas, (3) Cysts, (4) Astroblastomas, and (5) Mixed tumors.

1. Teratomas-These tumors arise almost exclusively in young males from four to sixteen years of age, although exceptions to this has been reported. These are also associated with precocious secondary sexual development, otherwise known as pubertas praecox or macrogenitosomia praecox. Bing[4] in 1938 gave a very comprehensive survey of this condition. A brief description of teratomas is summarized below.

The tumor tissue is seen to contain a variety of histoid structures, among which epithelial elements predominate. There are islands of stratified squamous epithelium (epidermoid) with a moderate degree of keratosis. In focal areas hair follicles are observed. Epidermoid cysts, which vary considerable in size, are common. In many places the epithelium lining these cysts are piled up several layers in thickness, and the contents are composed of desquamated epithelial cells. Other cysts are lined with granular epithelium, its cells being high columnar and mucus producing. Here and there, the epithelium is papillary and several layers in thickness, and the sub-epithelial tissue is composed of very cellular embryonal mesenchymal tissue. The content of the cysts is amorphous material containing single polymorphonuclear leukocytes and chromatin debris. In some places organoid structures resembling intestine is seen. These consist of many mucus producing glands overlying a densely cellular mesenchymatous stroma, which in turn lay on a stroma that is loose and fibrillar. This mucosa and submucosa is enveloped by two distinct layers of smooth muscle, an inner layer of circular fibers and an outer layer of longitudinal fibers. In other places the epithelium closely resembles that of the upper respiratory passages, and islands of cartilage and bundles of smooth muscle fibers give the structure a bronchus-like appearance.

Mesodermal derivatives are plentiful, in the form of islands of cartilage, fat tissue, and striated muscle. There are islands of both cartilaginous and membranous bone formation, and between the bony trabeculae are thin-walled blood vessels and islands of active bone marrow.

Neurogenic elements are present in a variety of histoid forms, the most prominent being neuroepithelial tubules composed of large cells with an ample amount of cytoplasm and large oval vesicular nuclei. The inner border of the cells is the site of a distinct cuticular membrane, and there are granules of blepharoplasts just beneath it. In other places there are structures resembling medullary epithelium. Much of this is arranged in the form of tubules, the cells being columnar and hyperchromatic. Innumerable cilia protrude into the lumen from the lining cells. In addition to the embryonal nerve tissue, there are focal accumulations of large, fully developed ganglion cells, each of which are enveloped by a zone of capsule cells similar to that seen in the spinal ganglia.[44][47][23][4][5]

2. Pinealomas-These tumors arising from the pineal gland tend to resemble the structure of the developing pineal at some definite stage of its development. The more primitive the type that is found in these tumors, the more rapidly growing and more invasive the growth. The primitive type of such tumors is termed a pineoblastoma. These tumors are seen most often in young adults, and the course is usually short-less than a year. The description following is that of a typical pinealoma.

The histological structure of the pinealomas is extremely variable since it consists of cells of two distinctly different types each of which may show individual pleomorphism along with a quantitative difference in the ratio of the cells of one type to the cells of the other. The tendency of the cells to show a characteristic morphological arrangement is quite variable, but is liken to a mosaic pattern.

A typical pinealoma is now described. There is present a moderately cellular tissue composed of large cells with intermingled small cells, showing no characteristic arrangement in many places but resembling a mosaic pattern in others. A moderately abundant connective tissue stroma is scattered diffusely throughout the tumor. The large cells show marked pleomorphism and no consistently characteristic shape. Some are nearly round with scant cytoplasm and measure up to 30 microns in diameter; while others are elongated with abundant cytoplasm. The nuclei of the large cells are usually round or vesiculated with a prominent nucleolus and the chromatin heavily concentrated at the nuclear membrane. Mitotic figures are usually observed in the large cells. The small cells are indistinguishable from lymphocytes. They show moderate pleomorphism and vary in size from one closely resembling a large lymphocyte with a moderate amount of cytoplasm and a nucleus with reticulated chromatin to one resembling a small lymphocyte with scant cytoplasm and a deeply chromatin nucleus. No mitotic figures are observed in the small cells.[59][26][45][30][36][21][61][27]

3. <u>Cysts</u>-Cystic developments within the pineal body are generally of three types: (1)small, single or multiple cavities which do not cause an enlargement of the gland and are found in as high as 30% of pineal bodies examined,[6] (2) cysts associated with pineal tumors, particularly, teratomas and pinealomas; (3) cysts unassociated with tumors which are sufficiently large to distend the gland and cause pressure symptoms.

The theories of the origin of pineal cysts are as follows: (1) lacunae of glial degeneration, (2) glial lacunae secondarily invaded by ependyma, (3) abnormal dilatation of glandular acini, (4) ependymal invagination, and (5) artificial cavities produced by enucleation of acervuli.

The wall of a typical cyst shows a central area of excavation where the fluid in the cyst has been discharged. Within the cyst wall there is amorphous protein debris, just outside of which there is a layer of glial tissue. Outside of this are a few pineal cells and the peripheral capsule is formed of rather dense fibroblasts. There is no evidence of malignancy, of teratoid derivation, or of corpora arenacea, as a rule, among the pineal cells.[43]

4. Astroblastoma-These tumors resemble the primitive pinealomas but are characterized by the presence of neuroglia cells. These tumors are more commonly found in adults nearing middle age. The course is short, also.

The outer portion of the tumor is composed of loose, fibrillary connective tissue with many small and large dilated vascular sinuses. In one area a small remnant of tissue of the choroid plexus is seen invaginating the mass, and scattered about are laminated calcareous concretions. The stroma of the remaining portion is more compact with numerous blood vessels and connective tissue. The thickened walls of the vessels often reveal a fine radial fibrillation and in places extend for a short distance between the adjacent cells. The endothelial cells of the vessels are swollen. Occasional plasma cells are seen in the connective tissue. Between the vessels are many loosely scattered, rounded or irregular angular cells with short, slender, protoplasmic processes, which form a delicate and loose network. These cells tend to arrange themselves about the blood vessels. The nuclei are round and oval, containing a moderate amount of chromatin. There are small patches composed of fibrillary glia. Occasional astrocytes and unipolar and bipolar spongioblasts are seen. Most of the cells and their processes show marked regressive changes such as pyknotic nuclei and vacuolation of their cytoplasm. Elements of the normal pineal body are not definitely demonstrable in the tumor.[70]

5. Mixed tumors-These tumors are found at all ages, but as a rule the course is relatively short. The name of this class of tumors is admittedly a misnomer, but all of the remaining types of pineal tumor are listed under this classification. These would include

psammomas,[70] melanosarcoma, and cholesteatomas. A typical mixed tumor is described below.

In general the tumor is cystic and composed of mesenchymal tissue in the form of hyaline cartilage surrounded by connective tissue, choroid epithelium, neuro-epithelial tissue and pigmented epithelial cells.

The outer surface of the tumor is surrounded by a layer of loose, fibrillary connective tissue. This connective tissue contains elongated, oval or round nuclei with fine and coarse chromatin granules, and small laminated layers of calcareous concretions. The loose stroma contains many dilated blood vessels and spaces filled with protein coagula and occasionally with red blood cells. Sharply demarcated islands of well developed hyaline cartilage cells are occasionally present near cyst like structures, which are lined by a single layer of cuboidal epithelial cells and are surrounded by connective tissue. Extending from the outer fibrillary connective tissue layer are cauliflower-like, out-branching villi with many collaterals, some of which are broad and others narrow. Blepharoplasts are not demonstrable in these villous structures as a rule.

Other areas contain primitive spongioblasts, oval and cylindric, with chromatin granules in the nuclei.

These cells are arranged about clear spaces in the form of rosettes. The lining of the spaces is formed by the inner surface of the primitive spongioblasts. The rosettes simulate the central canal of a developing neural tube and are concentrically arranged closely together. The canals are lined by a distinct cuticular membrane which contain numerous minute, dark stained, round, rod-shaped bodies, resembling blepharoplasts. Scattered in other places are single layers of columnar epithelial cells with round nuclei and an abundant cytoplasm forming the lining of large cavities. The inner surface of these cells contain numerous rod-shaped to needle-shaped bodies of melanotic pigment, arranged serially and parallel to the long axis. Mitotic figures are not present usually.

SYMPTOMATOLOGY and DIAGNOSIS

Enlargements of the pineal gland usually present clinically a well-defined syndrome. Owing to the anatomical position, enlargements of the gland cause pressure on structures which give rise to clear-cut clinical symptoms and hence are quite early recognizable.

The symptoms can best be considered under three headings: (1) Focal-those due to the lesion itself. (2) Local-the changes brought about within the central nervous system. (3) General-the somatic changes which sometimes accompany such enlargements.

1. Focal Signs-The focal signs which may be produced by tumors are due in the main to the anatomical position of the gland. It is because of its relationship to the superior corpora quadrigemina that the eye signs produced are so characteristic.

The aqueduct of Sylvius lying below the gland is very liable to be occluded and produce a severe degree of internal hydrocephalus when pressed upon by a pineal tumor.

The cerebellum lies immediately posterior to the pineal and is often invaded by growths arising in the neighborhood.

A contributory factor in the production of the internal hydrocephalus is the fact that the vein draining the choroid plexuses-the vein of Galen-is very liable to be compressed, with the result that engorgement of the choroid plexuses is produced and possibly an increased secretion of the cerebrospinal fluid.

Eye Signs.-Tumors may extend into the corpora quadrigemina and oculomotor region and produce a clinical syndrome which is characterized by loss of pupillary reaction to light, reaction to accommodation, and upward, downward, and lateral movement of the eyes, in that order of development. It is extremely common to find that the light reflex is absent and the patient unable to look upward. Disturbances of fixation of gaze, ptosis, and anisocoria may be explained by compression of the superior colliculi and underlying oculomotor system. Diplopia is a frequent occurrence, readily explained by the effect of the tumor on the oculomotor nuclei. Argyll Robertson pupils, an almost pathognomonic sign, pointing to the disruption of the quadrigeminal plate, is frequently encountered. Skew deviation is a fairly common finding and is associated with the envolvement of the brachia conjunctiva.

Ear Signs.-Should the inferior corpora quadrigemina be pressed upon, then deafness, unilateral or bilateral, complete or partial, may result.

Cerebellar Signs.-Extension occurs into the cerebellum. This may be into either hemisphere or directly in the midline.

Nystagmus is very common; there is often giddiness and incoordination, with a tendency to swerve to the side most affected, or, if in the midline, a tendency to fall backward. There is weakness, adiadochokinesia, intention tremor in the arms, and usually a grossly ataxic gait. Rombergism may be present. The cerebellar involvement will in some cases also give rise to a dysarthric speech, usually staccato in type.

Other cerebellar signs may be present. On extension of the hands there is a tendency to fall away on the side of the lesion. The past-pointing test may show deviation.

The reflexes may be diminished or absent on one or both sides and the limbs atonic, but usually the pyramidal involvement predominates.

Pyramidal and Sensory Signs.-The pyramidal tracts and medial lemnisci may be affected. Involvement of the pyramidal tracts gives rise to increase in tone on the affected side, weakness, increased deep reflexes, absent abdominal reflexes, and an extensor plantar response. The sensory changes take the form of a hemianaesthesia, as all the sensory fibers at the level of the corpora quadrigemina have joined the medial lemniscus.

Signs of Third Ventricle Involvement.-The somatic changes sometimes associated with pineal tumors have been referred to involvement of the hypothalamus and third ventricle.

Disturbed temperature regulation has been reported in a few cases of pineal tumor. The hypothalamus is probably concerned in the control of body temperature, and the case reports show that there may be rise of temperature of an irregular type without any apparent source of infection and with no corresponding rise in pulse rate. The controlling center in the hypothalamus itself or its efferent pathway may be damaged. Polyphagia, polyuria, and glycosuria have also been observed, and are probably due to hypothalamic involvement.

Signs of Involvement of the Cerebral Hemispheres.-As a pineal tumor grows, extension occurs upwards into the hemispheres. It is of necessity a deep extension, and the motor cortex and sensory cortex are not usually involved. The optic radiations, however, pass near by on their way to the occipital cortex, and these may be cut through and a right or left homonymous hemianopia result.

2. Local Signs.-Owing to the site of the lesion, signs due to raised intracranial pressure manifest themselves early in the course of the tumor growth. Headaches are severe and continuous, and are associated with vomiting. Mental lethargy and reduction in mentality may be early signs, as may also giddiness. Loss of vision occurs from the effects of papilloedema, which is usually very marked and presents itself as a very early sign. Epileptiform fits also occur.

Signs are produced in the cranial nerves as the result of the raised intracranial pressure. The third ventricle is commonly affected, and double vision and strabismus are frequently present. The VIth nerve is also involved. There is paralysis of the external rectus on either or both sides, with a convergent strabismus. The olfactory nerve is not affected. The Vth nerve may be affected, giving rise to a weakness of the muscles of mastication and sometimes sensory loss on that side of the face.

Facial paralysis is seen quite commonly, and is either produced by the local extension of the growth or from damage to the nerve resulting from the raised intracranial pressure.

Deafness is common, and has already been mentioned.

The nerves IX, X, XI, and XII are not usually affected; only if the cerebellum is extensively invaded will they be pressed upon and give rise to their characteristic physical signs.

3. General Signs.-Pineal tumors associated with general somatic changes are almost confined to the male sex. The disturbances of growth associated with pineal tumors affect chiefly the genital organs, but are often associated with adiposity and sometimes with general and symmetrical overgrowth.

Hypertrophy of the penis and testes, with growth of pubic hair and precocious sexual instinct, have been observed with most tumors classed as teratomas, as well as with simple, benign, and malignant tumors. The testicles show a marked increase in the size and number of the interstitial cells. The breasts enlarge, and one case has been reported of a secretion of colostrum in a boy aged 4 yrs., associated with testicular enlargement.

Increase of hair occurs also on the lips and chin and in the axillae. Deepening of the voice may take place.

The adiposity which occurs has been observed with all varieties of pineal tumors, and cannot be distinguished clinically from hypophyseal obesity. The adiposity is proximal in distribution; it is marked over the shoulders and pelvic girdles, with considerable enlargement of the breasts. The buttocks, thighs, and abdomen also show heavy deposits of fat. The incidence of pubertas praecox in verified cases of pineal tumor is not as great as formerly assumed. The internal hydrocephalus seen often in such tumors is due to the blockage of the aqueduct of Sylvius. The coincidental dilatation of the third ventricle results in alterations in the hypothalamus, the part of the brain stem concerned with regulation of the vegetative functions. This factor explains the relative infrequency of pubertas praecox, a disturbance of sex character, by pointing out that the condition of macrogenitosomia praecox is merely an abnormal expression of the vegetative system.

The possibility is that the pineal gland normally facilitates growth in general, and sexual development in particular. Acceleration of these functions occurring in the course of pineal tumors may therefore be interpreted as hyperpinealism. In the absence of further data, obesity and hypertrichosis may be considered as part of the general and sexual overgrowth, but the hypophyseal failure must be considered as a possible contributing factor in the adiposity.

Displacement of the calcified pineal gland is of considerable aid in localizing a brain tumor. Hence, X-ray plays a part in the diagnosis of pineal tumors, tumors of the parapineal area, or tumors of other parts of the brain, the latter of which may be divided into supratentorial and subtentorial tumors. For example, if the pineal body is displaced upward, the lesion is probably beneath the pineal gland; if the displacement is lateral, the tumor is usually to the right or to the left. The errors resulting from the use of any of the methods for determining pineal position may be either intrinsic to the method itself or be due to the lack of familiarity with the method, inexperience, or the result of human fallibility. In considering the intrinsic errors of the various methods, it is important to remember that displacement of the pineal can only be detected when the displacement has been sufficient to crowd the pineal body beyond the confines of the normal zone. Also, one must not assume that the center of calcification does not represent the center of the pineal mass.

There are four methods now in use, namely, the Vastine and Kinney[65] or graphic method, the Dyke[15] modification of the graphic method, the proportional method,[19] and the cranioangle method.[20] The graphic method with the Dyke modification requires measurements with a rule and consultation with standard graphs. Errors are due to: (1) Nonproportional character of graph, producing errors in dolichocephalic and brachycephalic skulls, (2) Constant width of normal band, (3) Variations in skull shape. The errors of the proportional method are due to variations in skull shapes. The cranioangle method produces errors due to difficulty in identification of points on skull. The latter two methods, according to literature, give the highest percentage of successful determination of pineal displacement, but the method to use is left up to the individual roentgenologist.

The advantage of determining pineal displacement becomes valueless in the diagnosis of pineal tumor when one realizes that most of the present day methods are dependent upon pineal calcification, a post adolescent development, and fully half of the tumors of the pineal body are in preadolescent or adolescent persons. However, the new cranioangle method does not use such a basis for determination of pineal displacement so it may be more adaptative than the older methods.

TREATMENT

Although it is possible to operate on the pineal body using local infiltration of the scalp and some scopolamine and morphine, it is considered preferable to use rectal avertin, local infiltration of the scalp with ½% novocain, and to follow with intratracheal gas and oxygen. The latter step is desirable in that the patient should be completely quiet while the deep approach to the pineal is done and should the patient quit breathing, oxygen or carbon dioxide can be given, a very good precaution when operating near the brain-stem, where slight deflections in either direction may press or drag upon the respiratory center.

In surgery on the pineal body, there are only two approaches to the pineal that are of any practical value. Dandy's[10] operation is the present method of choice and is based on experimental procedures performed on dogs. After the preliminary infiltration of the scalp with novocain, a large right occipito-parietal osteoplastic flap is fashioned and bleeding controlled. Bleeding vessels in the dura mater are underrun with silk sutures, while those occurring in the bone are controlled with a bone wax.

A flap of the dura mater is turned outwards on top of the osteoplastic flap, and bleeding from the cut surface of the dura is stopped by silver clips or ligatures. The lateral ventricle is then tapped at the junction of its body and descending horn; the cerebrospinal fluid being allowed to flow away over the brain. The needle is left in situ for as long as possible to ensure complete evacuation of the ventricle. The cerebral veins, running from the upper part of the hemisphere into the superior sagittal sinus and numbering five or six, are now divided and secured between fine ligatures or silver clips. Injury to the vein, draining the Rolandic area of the brain, should be avoided or a transient hemiplegia may result. Now the whole of the posterior extremity of the hemisphere is retracted so as to expose the falx cerebri. Continued retraction will bring the inferior longitudinal sinus into view. Below it lies the corpus callosum, but it may be necessary to divide the inferior longitudinal sinus and slit the lower edge of the falx for a half an inch or more to give sufficient exposure of the splenium of the corpus callosum.

The splenium is then excised in the midline and the tumor is exposed. The most important structure in relation to the tumor is the great vein of Galen, lying under the fornix, and this with its tributaries must be preserved. Having exposed the tumor, it is then pried out of its bed by means of a curved dissector. Absolute hemostasis is essential, and all bleeding points may be controlled by silver clips or the use of a diathermy point. Also, the tumor bed must be dry before completion of the operation.

In closure, the posterior portion of the cerebral hemisphere is dropped back in place, and the dura mater is tied with several tethering sutures. Drainage by means of a fine, corrugated dam is often necessary for a day or so. The osteoplastic flap is replaced and the scalp secured by two layers of sutures. The head is bandaged; the patient is kept flat for the first three days, then allowed a pillow. Fluid balance is maintained by an adequate intake, rectally or intravenously. The stitches are removed on the tenth day and consequently the patient is allowed up and around.

The second method of approach is that devised by van Wagenen,(64) in which the tumor is attacked through the medial wall of the lateral ventricle. It is an easier method and the route is less vascular. The tributories of the great vein of Galen are more easily seen and handled, too. However, this method may leave some permanent disturbance of function in the form of hemiplegia and homonymus hemianopia.

The first portion of the operation is practically identical to Dandy's approach. The dura mater is incised, and a flap is turned downward. A reversed L-shaped incision, 6 cm. in length, is made in the cortex, extending from the posterior end of the superior temporal lobe gyrus, upward and slightly backward, ending in the lobus parietalis superious. This incision is gradually deepened by means of the diathermy cautery, using the cutting and coagulating currents alternately. The edges are retracted by means of small flange retractors covered with moist lint. The incision is deepened until the dilated lateral ventricle is opened. The bulging medial wall of the ventricle, covered in part by the choroid plexus, may be seen. The medial wall of the ventricle is then gently incised, and the pineal tumor is exposed.

This is gradually separated from its site. Absolute hemostasis is procured, and a small piece of rubber dam is inserted for drainage. The dura mater is replaced with stitches, the osteoplastic flap is replaced accurately, and the scalp is united by a double layer of interrupted sutures. A firm dressing is then applied. The drain is removed after twenty-four hours, and the stitches on about the tenth day.

Post-operative x-ray therapy is a wise precaution for the patient as most pineal tumors are radiosensitive. Ventricular puncture may be necessary during convalescence if the intracranial pressure increases.

CONCLUSION

This thesis has covered all of the main fields of medical research upon the pineal body. An attempt to condense the older, known facts and to enlarge upon the data brought forth in the past three decades has been the principal aim in the presentation of this thesis. In reviewing the literature, little known facts and new developments have greatly changed my comprehension of the pineal gland.

In considering the history of the pineal gland, it is interesting to note that it had been known in the days of ancient Greeks and since the birth of medicine. Present evidence definitely associates the pineal gland as an active median third eye in the lower forms of vertebrates. In the higher forms, it is vestigial structure, generally considered as a non-functional gland, but possessing the anatomical features of a functioning organ early in its development.

The human pineal body first makes its appearance as a diverticulum in embryos of approximately 15 mm. in length. It is easily identifiable by the third or fourth month of fetal life. At this time active proliferation of cells causes a hyperplasia effect and enlargement of the gland. Glandular structure is seen in the pineal body in this period of growth. Later these disappear and the body undergoes a certain amount of atrophy and calcification.

Neuro-epithelial cells give rise to the typical parietal cells, and mesenchyme cells form the basis for the high vascularity of the structure. The typical appearance of the pineal body in young children is that of a mosaic pattern of alternating light and dark cells. In adults the pineal has changed to a rather indefinite pattern of alveolar cells, nerve cells, and connective tissue cells.

Nerve fibers of the pineal body belong to the sympathetic nervous system and are both fine and coarse in nature. The arterial blood supply is received from the superior cerebellar artery. The basal vein forms the venous drainage of the pineal body.

The experimental and clinical evidence with respect to the function of the human pineal body is at the present time too conflicting to allow any definite conclusions to be made. However, during the past three decades, advancements in the action of the pineal body has been made compared to the data known in the past three hundred years that I feel certain it will not be long in the future before sufficient evidence one way or another is found. I personally believe that the evidence will point towards the pineal body being a functional gland with hormonal properties at least early in the life of a child.

Tumors of the pineal body are found more often in young children than many other brain tumors. They are also found in adults, however, and usually present symptoms common to any brain malignancy. The tumors as a rule are rather sensitive to x-ray and are short in course. Certain types of pineal tumors have a curious, unknown, high relationship to the syndrome known as macrogenitosomia praecox or pubertas praecox.

In the past three decades the symptomatology of pineal tumors has become more definite. It is characterized by raised intracranial pressure, rather severe headaches, definite eye signs and loss of eye movements, vomiting, epileptiform fits, and possible mental degeneration.

The surgery of the pineal organ, although yet in its infancy, may be said to be advancing owing to the fact that neurological diagnosis becomes more established and more accurate each year, and that standardization of operations have occurred. The majority of pineal tumors are radio-sensitive, hence, x-ray is of therapeutic value besides an important diagnostic aid.

BIBLIOGRAPHY

1. Aschoff, L. Lectures on Pathology New York Paul B. Hoeber, Inc. 1924 p. 101

2. Anderson, D.H. and Wolf, A. Pinealectomy in Rats with Critical Survey of Literature J. Physiol. 81:49-62 March 29, 1939

3. Aronstan, N.E. Pineal Gland in Relation to Sexual System Medical Record 144:494-496 Dec. 1936

4. Bing, J.F. et.al. Pubertas praecox; Survey of Reported Cases and Verified Anatomic Findings J. Mt. Sinai Hosp. 4:935-965 Mar.-Apr. 1938

5. Bochner, S.J. and Scarff, J.E. Teratomas of the Pineal Body Arch. of Surgery 36:303-329 February 1938

6. Carr, J.L. Cystic Hydrops with Report of Six Cases J. Nerv. and Ment. Diseases 99:552-572 May 1944

7. Clark, W.E.L. Pineal Gland; Nervous and Vascular Relations J. Anatomy 74:471-492 July 1940

8. Cleghorn, R.A. et.al. Hypogonadism Associated with Invasion of Mid Brain and Hypothalamus by Pineal Tumor Quart. J. Med. 7:183-209 Apr. 1938

9. Cooper, E.R.A. Human Pineal Gland J. Anatomy 67:28-46 Oct. 1932

10. Dandy, W.E. Pineal Tumors; Operative Experience in Cases Arch. Surg. 33:19-46 July 1936

11. Davidoff, L.M. Pineal Tumors; Endocrine Aspect Surgery 16:306-314 August 1944

12. Davis, L. and Martin J. Results of Experimental Removal of Gland in Young Mammals Arch. Neurol. and Psychiat. 43:23-45 Jan. 1940

13. Davis, L. and Martin J. Syndrome of Destruction of Gland; Experimental Observations Arch. Int. Med. 67:1119-1128 June 1941

14. Del Rio Hortega, P. Pineal Gland, in Penfield, W.; Cytology and Cellular Pathology of the Nervous System, New York Paul B. Hoeber, Inc. 1933 Vol. 2

15. Dyke, C.G. Indirect Signs of Brain Tumor as noted in Routine Roentgen Examinations; Displacement of Pineal Shadow Am. J. Roentgenol. 23: 599-606 June 1930

16. Engel, P. Assay of Pineal Gland Extracts Endocrinology 25:144-145 July 1939

17. Fischer, E. Pineal Gland Preparations; Active Fraction Endocrinology 33:116-117 Aug. 1943

18. Fleishmann, W. and Goldhammer, H. Zur Erage der Hormonalen Wirkung der Zirbeldruse Klin. Wchnschr. 15:1047-48 1936

19. Fray, W.W. Comparison of Graphic and Proportional Methods in Proven Cases of Brain Tumor Radiology 30:579-587 May 1938

20. Fray, W.W. Methods for Determining Pineal Position with analysis of their errors Am. J. Roentgenol. 42:490-497 Oct. 1939

21. Friedman, E.D. and Plaut, A. Pinealocytoma with Meningeal and Neural Metastases Arch. Neurol. and Psychiat. 33:1324-1341 June 1935

22. Gerstley, J.R. Anorexia of Perplexing Origin; case of Teratoma M. Clin. North Am. 25:147-154 January 1941

23. Gerstley, J.R. et.al. Pineal Teratoma J. Pediat. 17:512-520 October 1940

24. Gladstone, R.J. and Wakeley, C.P.G. Anatomy, Histology, Development and Histogensis of Human Organ J. Anat. 69:427-454 July 1935

25. Gladstone, R.J. and Wakeley, C.P.G. The Pineal Organ First Edition Baltimore Williams and Wilkins 1-9, 299-326, 381-479 1940

26. Globus, J.H. Pinealoma Arch. Path. 31:533-568 May 1941

27. Globus, J.H. and Silbert, S. Pinealomas Arch. Neurol. and Psychiat. 25:937-985 May 1931

28. Gray, H. Anatomy of the Human Body Twenty-fourth Edition Philadelphia Lea and Febiger 1943 pps. 580 and 654

29. Grinker, R.R. Hypothalamic Functions in Psychosomatic Interrelations Psychosom. Med. 1:19-47 January 1939

30. Groff, R.A. Dissemination of Glioma by Extension at Distance; case of Pinealoma Am. J. Cancer 29:651-658 April 1937

31. Grollman, A. The pineal body and its Disorders Modern Med. 14 September 1946

32. Hanson, A.M. Pineal Gland Histology Minn. Med. 20:78-81 February 1937

33. Hawes, L.E. and Mead, S. Posterior Displacement of Calcified Pineal in Subtentorial brain tumors Radiology 40:367-370 April 1943

34. Horrax, G.H. and Bailey, P. Tumors of the Pineal Body Arch. Neurol. and Psychiat. 13:423-470 April 1925

35. Horrax, G. and Daniels, J.T. Pineal Tumors; Conservative Treatment S. Clin. North Am. 22:649-659 June 1942

36. Horrax, G. Pineal Tumors; Extirpation of Huge Pinealoma from Patient with Pubertas Praecox; New Operative Approach Arch. Neurol. and Psychiat. 37:385-397

37. Herren, R.Y. Reliability of Roentgenographically determined Pineal Gland shift in Brain Tumor Surgery 8:478-479 September 1940

38. Kahn, E.A. Pineal Tumors; Surgical Treatment Arch. Neurol. and Psychiat. 38:833-842 October 1937

39. Kasanin, J. Defense Reactions in Anxiety States of Central Origin Psychoanalyst Quart. 11:493-502 Oct. 1942

40. Krabbe, K.H. The Pineal Gland, Especially in Relation to the Problem of its Supposed Significance in Sexual Development Endocrinology 7:379-414 May 1923

41. Lawson, H. Pineal Gland; Present Status as Endocrine Organ Ky. M.J. 38:345-348 Aug. 1940

42. Levin, P.M. Pineal Gland; Nervous Structure in Monkey J. Comp. Neurol. 68:405-409 June 1938

43. Liber, A.F. Pineal Cysts; Cystic Hydrops J. Nerv. and Ment. Dis. 89:782-794 June 1939

44. Lichinstein, B.W. Pineal Tertoma; Clinicopathological Report Arch. Neurol. and Psychiat. 44:153-161 July 1940

45. Mackay, R.P. Pinealoma of Diffuse Ependymal Origin Arch. Neurol. and Psychiat. 42:892-902 Nov. 1939

46. McCord, C.P. The influence of the Pineal Gland upon Growth and differentiation with particular reference to its influence upon prenatal development. Surg. Gyn. Obstet. 25: 250-257 September 1917

47. McLean, A.J. Pineal Teratomas; with Report of case of Operative Removal Surg. Gyn. and Obst. 61:523-533 October 1935

48. Malek, S.A. Relationship between epiphysis cerebri and Reproductive System J. Anat. 73:419-423 April 1939

49. Maximow, A.A. and Bloom, W. Textbook of Histology Fourth Edition Philadelphia and London W.B. Saunders Co. 1942 pps. 329-332

50. Neale, A.V. Precocious Puberty with Report on case of Pineal Syndrome Arch. Dis. Childhood 13: 241-248 Sept. 1938

51. Pastori, G. Ein bis jetzt noch nicht beschriebenes sympathisches Ganglion und dessen Bezilhungen zum Nervus conari sowie zur Vena Magna Galeni Z.ges. Neurol. Psychiat. 123:81-90 July 1929

52. Pastori, G. Uber Nervenfasern und Nervenzellen in der "Epiphysis Cerebri" Z.ges. Neurol. Psychiat. 117:202-211 June 1928

53. Pratt, D.W. and Brooks, E.F. Pineal Tumors; Successful Excision Canad. M.A.J. 39:240-243 September 1938

54. Quercy, P. et.al. Epiphysis and Para-Epiphysial Formations in Adult Human Being Rev. Neurol. 69:483-490 May 1938

55. Rolleston, H.D. The Endocrine Organs In Health and Disease London Oxford Uni. Press 1936

56. Rowntree, L.G. et.al. Further Studies Ann. Int. Med. 9:359-375 October 1935

57. Rowntree, L.G. et.al. Role of thymus and pineal glands in growth and development N.Y. State J. Med. 36:1277-1283 September 1936

58. Rowntree, L.G. et.al. The Biological Effects of Pineal Extracts Endocrinology 20:348-357 May 1936

59. Russell, W.O. and Sachs, E. Pinealoma; clinicopathological study of seven cases with review of literature Arch. Path. 35:869-888 June 1943

60. Sharpey-Schafer, Sir E. The Endocrine Organs Second Edition London Longmans, Green and Co., Ltd. 1926 pps. 320-328

61. Stringer, S.W. Diabetes Insipidus associated with Pinealoma Transplant in Tuber Cinereum Yale J. Biol. and Med. 6:375-583 March 1934

62. Strong, O.S. and Elwyn, E. Human Anatomy Baltimore Williams and Wilkins Co. 1943 pps. 277-312

63. Sullens, W.E. and Overholser, M.D. Pinealectomy in successive generations of rats Endocrinology 28:835-839 May 1941

64. Van Wagenen, W.P. A surgical approach for the Removal of Certain Pineal Tumors Surg. Gyn. and Obstet. 53:216 1931

65. Vastine, J.H. and Kinney, K.K. Pineal Shadow as an aid in the Localization of Brain Tumors Am. J. Roentgenol. 17:320-324 Mar. 1927

66. Wade, N.J. Studies on Pineal Gland Function-Antigonado trophic and estrogenic potencies Endocrinology 21:681-683 Sept. 1937

67. Wakeley, C.P.G. Surgery of Pineal Organ Brit. J. Surg. 25:561-591 January 1938

68. Warren, S. Pineal Cancer; metastasis from breast Am. J. Cancer 28:713-719 December 1936

69. Weinberg, S.J. and Doyle, A.F. Effects of injected extracts of fresh pineal glands of cows on growth of immature white mice Proc. Soc. Exper. Biol. and Med. 28:322-323 December 1930

70. Zeitlin, H. Pineal tumors in region of Pineal body; clinicopathological report of three cases Arch. Neurol. and Psychiat. 34:567-586 September 1935