

1945

# Hypophysectomy and its physiologic effects in the pig (*Sus Scrofa domestica*)

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HYPOPHYSECTOMY AND ITS PHYSIOLOGIC EFFECTS IN  
THE PIG (SUS SCROFA DOMESTICA)

by

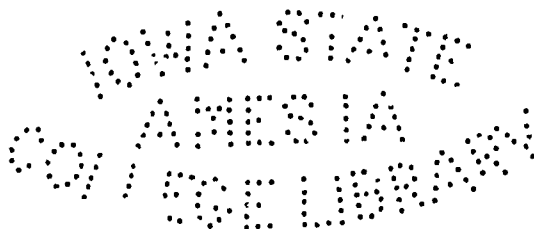
Lorenz Edward St. Clair

A Thesis Submitted to the Graduate Faculty  
for the Degree of

DOCTOR OF PHILOSOPHY

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Approved:



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## INTRODUCTION

Most of our present knowledge concerning the anatomy and physiology of the pituitary gland in mammals has come from work on laboratory animals, including the dog and cat. The abnormal functions of the gland have been studied in man. The larger domestic or farm animals have generally not been investigated. Although the structure and functions of the pituitary gland have been found to be similar in all the animals used, certain differences do exist. The pig apparently differs from the other animals in its fat and carbohydrate metabolism.

To thoroughly study the functional significance of a gland, animals from which it has been removed must be observed. In order to perform hypophysectomy, the structure and relations of the gland must be known.

This investigation was undertaken to establish the structure and relations of the pituitary gland of the pig, to develop operative techniques for its removal from living animals, and to determine the physiologic effects of hypophysectomy.

## REVIEW OF LITERATURE

### Anatomical

#### Location and constituents of the hypophysis

Many investigators have described the location and relation of the hypophysis cerebri or pituitary gland. They have given its location as the hypophyseal fossa or sella turcica. The clinoid process, diaphragma sellae, dorsum sellae and the cavernous sinuses have formed a membranous pocket containing the gland (Tilney and Riley, 1938). Sisson and Grossman (1938) described the hypophyseal fossa of the pig as a very deep fossa limited behind by a prominent dorsum sellae, which contained lateral projections, the posterior clinoid processes. Anteriorly its floor sloped upward to the optic groove. The dorsal extension of the dural sac (diaphragma sellae), which surrounded the gland, was found to be complete only in man. It was incomplete in the ox, small ruminants, the pig, the dog and the cat, and absent in the horse (Koller, 1922). Wislocki (1937) investigated the meningeal relations of the hypophysis cerebri in man, the rat, the rabbit, the cat, the dog and the monkey. He described a fusion of the gland's capsule, the dura and the periosteum. The subarachnoid space extended into the sella only a short distance anteriorly in the dog and cat, and not at all in man, the monkey and the rabbit. There also was no subdural space in the fossa. Schwartz (1936) had found the same situation in the dog.

Van Dyke (1936) arranged the parts of the pituitary body and their embryonic origin as follows:

Part	Embryonic Origin
Pars glandularis.....	Rathke's pouch of buccal ectoderm
Pars intermedia .....	Superior part of the caudal portion of Rathke's pouch
Pars tuberalis .....	Paired lateral lobes at the ventro-nasal end of Rathke's pouch
Pars neuralis .....	Infundibular process of the diencephalon

The term "pars anterior" ordinarily referred to the pars glandularis but could include part of the pars tuberalis. All the structures derived from Rathke's pouch were often called the pars buccalis. The term "pars posterior" commonly referred to structures posterior to the residual lumen of Rathke's pouch, and therefore included the pars intermedia, the pars neuralis, and often a portion of the pars tuberalis. Tilney and Riley (1938) called the anterior lobe the pars distalis and the portions derived from Rathke's pouch the pars glandularis. The anterior and posterior lobes were separated from each other, except toward the stalk, by the residual lumen of Rathke's pouch.

Herring (1908) classified mammalian pituitary glands into three groups: (1) the cat, which had a hollow posterior lobe with a complete epithelial investment; (2) the dog, which had a solid-bodied posterior lobe with an almost complete epithelial investment; (3) man, the monkey, the ox, the pig and the rabbit, with a solid posterior lobe, except a little at the neck, and an incomplete epithelial investment. He described colloid or hyalin bodies in the posterior lobe.

Loeb and Friedman (1933) gave the weight of the pars glandularis (anterior lobe) of the pig as 125 mg. According to Atwell and Woodworth (1926), the pars glandularis of the cat made up 75 per cent, the pars intermedia 16 per cent, and the pars tuberalis 9 per cent of the weight of the buccal portion of the gland. Stein (1933) stated that in the adult male rat the pars glandularis formed 82 per cent of the gland weight, the pars intermedia 6.7 per cent, and the pars nervosa 11 per cent. In the adult female rat, the proportions were 86, 3.4 and 7.1 (Stein, 1934). In the mouse, Saller (1933) gave the proportions as 70, 19 and 11 for the male, and 71, 19 and 10 for the female. Rasmussen (1939) tabulated the figures for the adult human male as 75, 2 and 23 for the pars distalis, pars intermedia and pars nervosa respectively. The percentages for the adult non-pregnant female were 80, 2 and 18. The whole gland weight was slightly greater during pregnancy.

#### Blood supply

Wislocki (1937) traced the vascular supply to the hypophysis in human embryos and fetuses. It was supplied by superior and inferior sets of arteries. Several superior hypophyseal arteries were derived from the internal carotid and posterior communicating arteries on each side. They branched into the infundibular stalk and anterior lobe and terminated in sinusoids. Inferior hypophyseal arteries of dural origin penetrated the neural lobe from each side near the midline and broke up into a capillary bed. The superior arteries were not accompanied by veins. The anterior lobe drained by various connections into the cavernous sinuses. Veins

coursed from the posterior lobe with the inferior arteries to enter the intercavernous sinus. Portal veins ran within the infundibular stalk and pars tuberalis to join the sinusoids of the pars distalis. The same arrangement was found in the rhesus monkey (Wislocki and King, 1936, and Wislocki, 1938), and in the cat (Wislocki 1937). Popa and Fielding (1930) stated that the portal veins drained toward the hypothalamus. Dandy and Goetsch (1911) believed that the pituitary of the dog was supplied by 18 to 20 arteries from the circle of Willis which ended as sinusoids in the anterior lobe. The sinusoids drained into a venous circle which lay as a satellite to the arterial circle. The pars intermedia was supplied from the infundibular stalk, brain and posterior lobe. The posterior lobe received a small artery which was formed by the union of branches from each internal carotid artery. One large vein and several small ones coursed from the posterior lobe to the cavernous sinus. Basir (1932) described a similar arrangement for the dog. He stated that portal veins coursed to the tuber cinereum.

#### Nerve supply

Among recent workers, Hair (1938) stated that the anterior lobe of the cat's pituitary gland received nerves directly by way of the blood vessels and indirectly by blood vessels through the pars tuberalis. The posterior lobe, including the pars intermedia, was supplied by fibers proceeding from the supraopticohypophyseal tract through the infundibular stalk. In the rat, Truscott (1944) found the anterior lobe to be only sparsely innervated. The fibers were derived from the infundibular tract

by way of the capsular sheath, hypophyseal fasciculi by way of the pars intermedia, and by way of small nerves accompanying the blood vessels. The nerves to the posterior lobe arose from the infundibular tract through the stalk in two fasciculi. The pars nervosa had the richest supply.

### Microscopic structure

Pars distalis (Pars glandularis). Three types of cells were usually recognized in the pars distalis (Schonemann, 1892): (1) reserve cells (chromophobes, neutrophils, chief cells); (2) oxyphils (eosinophils, acidophils, alpha cells); (3) basophilic cells (cyanophils, beta cells). The last two were often classified together as chromophils. They were named in general according to their staining characteristics.

Severinghaus (1933, 1937, 1938 and 1939) stated that the reserve cells, or chromophobes, were the stem cells. They were potentially either formers of acidophils or basophils. The acidophils and basophils could lose their granules and revert to the chromophobe type. Mitoses were rarely seen. Some of the earlier workers believed that the chromophobes were the parent cells but disagreed about the exact formation of the acidophils and basophils. Basophils have been described as sometimes arising from acidophils. The first cells to differentiate from the chromophobes in most mammals were the acidophils (Zimmerman, 1931, in the sheep and ox; Wolfe, Cleveland and Campbell, 1933, in the dog). The acidophils were thought to secrete the growth-promoting hormone, because in man acromegaly and gigantism were associated with oxyphilic tumors (Benda 1900). Smith and Smith (1923) produced growth-promoting effects by ox pituitary

tissue composed of oxyphils and reserve cells, but not by tissue composed of basophils and reserve cells. In certain dwarf mice, a complete absence of acidophilic cells was found (Smith and McDowell, 1930). The basophils were thought to influence the gonads. Following gonadectomy in the rat, the basophils increased in numbers and later became vacuolated (castration cells) (Addison, 1917). Smith, Severinghaus, and Leonard (1933) described an increase in basophils in the rabbit. Severinghaus (1932) did not find castration cells in the guinea pig. Rasmussen (1921) reported a basophilia in woodchucks during spring estrus. Others described conflicting results.

Smith and Dortzbach (1929) stated that growth stimulation was observed when pituitary glands of 90 to 100 mm. fetal pigs were implanted intramuscularly in hypophysectomized rats. Glands of 170 to 180 mm. fetal pigs stimulated the gonads of immature mice. The finding by Nelson (1933) of a predominance of basophils in the pars distalis of 70 to 100 mm. fetal pigs and a rise of acidophils at the 160 to 170 mm. stage indicated that in the pig the basophils influenced growth and the acidophils influenced the gonads. Cleveland and Wolfe (1933) described granule changes in both acidophils and basophils during the estrus cycle in the sow. The granule changes were greater in the basophils, however.

Rasmussen (1939) described the cells of the pars distalis in man as closely packed columns and irregular masses which were separated by prominent blood sinusoids and a small amount of connective tissue. Small acini with colloid could be found. The chromophobes made up 50 per cent of the cells in men and 52 per cent in women. The nucleus was vesicular



in structure. The cytoplasm stained only slightly and the nucleus often was the only part of the cell visible. The smaller cells were usually located in the interior of the cell columns. The acidophils, consisting of about 37 per cent of the cells in men and 43 per cent in women, were usually larger than the chromophobes. The cytoplasm was densely packed with prominent round, acid-staining granules. The nucleus was similar to that of the chromophobes. The acidophils were most numerous in the posterior two-thirds of each lateral half, leaving an acidophil-poor area in the center. The basophils were the largest in size and constituted about 11 per cent of the cells in men and 6 to 7 per cent in women. The granules were small and stained with basic dyes.

Maurer and Lewis (1922) recognized three chromophil and two chromophobe cell types in the anterior lobe of the pig. The third chromophil type was found in the dark anterior portion (pars tuberalis) of the anterior lobe. Nelson (1930 and 1933) gave a thorough description of the anterior lobe cells of the pig. The eosinophils were usually smaller than the basophils but had larger granules. A clear area was sometimes found in the cytoplasm of the basophils near the nucleus. The basophils were evenly distributed, except near the point of origin of the tuberalis, where they were most numerous. The acidophils were most numerous in the caudal half. The chromophobes stained faintly basophilic and were located more toward the centers of the cell cords.

Cleveland and Wolfe (1933) described cyclic cellular variations in the sow. In sexually immature pigs, 35.6 per cent of the cells were acidophils; 31.7 per cent were basophils; and 32.5 per cent were chromophobes.

The basophils had more granules during proöstrus and less during estrus and in the early stages in the development of the corpus luteum. Acidophils were more numerous and chromophobes less numerous in sexually mature than they were in sexually immature females.

The cytology of the anterior lobe of the guinea pig's pituitary was discussed by Kirkman (1937). The acidophils had coarse granules and a darker nucleus than the chromophobes. They were distributed more to the lateral than central parts of the lobe. Some of the basophils were large and dark blue; others were large or small and light blue. They were most numerous near the tuberalis and in the central area. A row of columnar ciliated cells was located anterior to the residual lumen toward the ventral part of the gland. More dorsally they became non-ciliated cuboidal in type. In the adult male 42 per cent of the cells were acidophils, 18.7 per cent were basophils and 39.5 per cent were chromophobes. In the diestrous female the count was 48.1, 16.7 and 35.2, and in the estrus female it was 46.9, 9.6 and 44.

According to Wolfe, Cleveland and Campbell (1933), the canine pars distalis had two types of basophils. In sexually immature dogs 59.7 per cent of the cells were acidophils, 3.7 per cent and 7.2 per cent were basophils, and 29.4 per cent were chromophobes. No basophils were present until after birth. Slight variations occurred during the estrus cycle and pregnancy. White and Foust (1944) gave the cell counts in young male dogs as 47 per cent acidophils,  $4\frac{1}{2}$  per cent basophils and  $48\frac{1}{2}$  per cent chromophobes. In females the counts were 48,  $4\frac{1}{2}$  and  $49\frac{1}{2}$ .

In castrated rats the acidophils were most plentiful in the central portions of the anterior lobe and surrounding the cleft (Nukariya, 1926).

The basophils were more peripherally located, especially where the intermedia joined the distalis. This view seems to be different from that found in other animals. He gave the count as 31.4 per cent acidophils, 14.1 per cent basophils and 54.5 per cent chromophobes in the male. In the female the proportions were 31.6, 15.5 and 52.9. According to Wolfe and Cleveland (1933) and Wolfe (1935), one type of basophil was present in rats. Slight cyclic variations were also described. The chromophobes were the most numerous cell type. A similar situation was present in rabbits except that the acidophils were the most numerous (Wolfe, Phelps and Cleveland, 1933).

Smith and Smith (1923) stated that in the bovine anterior lobe the central area was more basophilic and the lateral areas were more acidophilic. Spaul and Howes (1930) were in accord with this finding.

Warbritton and McKenzie (1937) described nine different types of cells in six fundamental groups in the anterior lobe of ewes in different stages of reproduction. Their classification was based mainly on granule changes.

Dawson (1937) named a special anterior zone of the pars distalis in the cat and rabbit, the zona tuberalis, since it consisted largely of chromophobes and basophils. This zone was very responsive to changes in the reproductive cycle.

Other constituents of the hypophysis. The pars tuberalis consisted of length-wise running anastomosing strands of small indifferent staining or slightly basophilic cells in the human (Rasmussen, 1939). Colloid vesicles, connective tissue strands and sinusoids were numerous. Nelson (1933) mentioned cysts in the pars tuberalis of the pig.

The pars intermedia was made up of a stratum of cells and intervening vesicles containing colloid and debris. Some of the basophilic cells invaded the pars nervosa (Rasmussen, 1939). Maurer and Lewis (1922) stated that two types of cells were present in the pars intermedia of the pig, a secretory cell and a small colloid-producing cell.

Bucy (1930) called the neuroglia-like cells of the pars nervosa of the ox "pituicytes." No true nerve cells were found there. Herring (1908) described amorphous masses in the pars nervosa of most animals. Gersh and Tarr (1935), however, believed that these were artefacts. Non-myelinated nerve fibers were numerous.

In the ox a glandular cone attached to the pars intermedia projected through the cleft into the pars glandularis where it attached by connective tissue (Wulzen, 1914).

Kingsbury (1942) stated that a pharyngeal hypophysis was present in a high percentage of cases in dogs. In hypophysectomized dogs its presence did not affect the symptoms of pituitary deficiency. He concluded that in the dog and man the pharyngeal hypophysis probably has no physiological significance.

### Hypophysectomy

#### Operations

Hypophysectomy has been performed on many animals both cold- and warm-blooded. It has been accomplished in at least ten different mammals: the cat, the dog, the ferret, the goat, the guinea pig, the hedgehog, the

monkey, the mouse, the rabbit and the rat. A number of different methods have been used by various investigators. The structural characteristics of each animal made certain operative techniques more convenient than others. The transbuccal, parapharyngeal and temporal routes of approach to the gland were usually employed.

Transbuccal (oral, buccal) method. The mouth was opened as far as possible. The soft palate was incised and the base of the skull exposed. After the bone directly adjacent to the pituitary gland had been bared, a hole was made through it usually by means of a trephine or dental burr. The duro-periosteal sac was opened and the gland was removed by suction or by forceps.

Parapharyngeal (retropharyngeal) method. An incision was made in the mid-ventral area. The larynx and pharynx were pushed aside and the bone exposed. The technique then followed that of the buccal approach. A tracheal tube was usually necessary to allow normal breathing.

Temporal (transtemporal, intracranial) method. An incision was made over the temporal area. The temporalis muscle was incised and laid back to expose the bone in the temporal fossa. An opening was made through the bone by means of a trephine or dental drill. The dura mater was then incised and the brain pushed aside to expose the gland, which was removed by suction or by forceps.

Some of the workers have employed other techniques such as orbital and auditory approaches, nasal trochars, orbital electrodes, cautery, high frequency currents, acid, hot wax and X-rays.

Table 1

Hypophysectomies as performed by different investigators

Animal	Approach	Author	
Dog	Temporal	Horsley 1886	
		Paulesco 1907	
		Cushing and Homans 1909	
		Crowe, Cushing and Homans 1910	
		Bell 1917	
		Dott 1923	
		Ascoli and Legnani 1912	
		Sweet and Allen 1913	
		Dandy and Reichert 1925	
		Koster and Geesink 1929	
		Karlik and Robinson 1931	
		Transbuccal	Aschner 1912
			Brown 1923
			McLean 1928
Transbuccal & Temporal	Camus and Roussy 1922		
Rat	Parapharyngeal	Smith 1927, 1930	
		Richter and Wislocki 1930	
		Thompson 1932	
		Wehefritz and Gierhake 1932	
		Möller-Christensen 1933	
		Anselmino and Pencharz 1934	

Table 1 (continued)

Animal	Approach	Author
	Temporal	Giragossintz 1934
	Auditory canal	Koyama 1930
Mouse	Parapharyngeal	Selye, Collip and Thomson 1933 Thomas 1938
Guinea pig		McPhail and Parkes 1933 Anselmino and Pencharz 1934
Hedgehog	Parapharyngeal	McPhail and Parkes 1933
Rabbit	Transbuccal	Smith and White 1931 White 1933
	Orbital	Firor 1933
	Nasal trochar	Kosakae 1930
	Hot wax	Krieser and Partos 1935
	Radon	Lacassagne and Nyka 1934
	X-ray	Mogilnitzky 1928
	Temporo-sphenoid	Harris and Popa 1937
Ferret	Parapharyngeal	Hill and Parkes 1932
Cat	Transbuccal	Gemelli 1908 Camus and Roussy 1922
	Transbuccal and Retropharyngeal	Allen and Wiles 1932
	Parapharyngeal	McPhail 1935
	Orbital electrode	Dott 1923
Goat	Parapharyngeal	Hill <u>et al</u> 1935
Monkey	Temporal	Firor 1932
Pig		Robinson 1937

Methods other than transbuccal, parapharyngeal and temporal have often failed to remove all of the gland and to remove it without injuring other structures. The techniques have been varied slightly by the different workers. Smith (1930), in approaching the bone from the parapharyngeal region, entered the nasal cavity, whereas Richter and Wislocki (1930) did not incise the pharyngeal wall. The former worker trephined the bone while the latter operators used a dental drill. Most of the operators used suction to remove the gland, whole or piece by piece. Hill et al (1935) destroyed the gland and controlled hemorrhage by means of a high frequency current. Aschner (1912) sealed the bone opening with gutta-percha dental compound while others allowed it to remain open. The parapharyngeal technique usually required a tracheal tube. White (1933) compressed the nasal mucosa thoroughly before exposing the bone. Smith (1930) used the temporal operation to inject chromic acid into the pituitary area. Dott (1923) often inserted a platinum plate into the fossa to remove the anterior lobe. Crowe, Cushing and Homans (1910) believed that the brain could be pushed to one side more readily if an opening were also made in the opposite temporal fossa. The use of a hypertonic salt solution, as recommended by Weed and McKibbin (1919) and Harris and Popa (1937), often helped to shrink the brain to allow more exposure of the gland for the temporal approach. The removal of the zygomatic arch also increased the size of the temporal operative area.

### Effects

The dogs operated upon by Horsley (1886) apparently lived for months



after the removal of the pituitary gland. Paulesco (1907), Cushing and Homans (1909), Crowe, Cushing and Homans (1910), Bell (1917) and Dott (1923) thought the gland to be essential to life since their dogs died usually in 24 hours to 3 weeks. Lassitude, cachexia, coma and even convulsions preceded death. Most of the workers, however, believed that hypophysectomized animals might live for long periods if hemorrhage, infection and brain injury were avoided. The life span of operated rats was about one-half that of normal animals (Smith, 1930). The symptoms observed following total removal of the gland were caused by the absence of the pars glandularis. Aschner (1912) concluded that hypophysectomy in the dog was physiologically complete if no remnants of the pars glandularis could be found grossly. If one-third of the pars glandularis remained, no symptoms of pituitary deficiency appeared. Smith (1930) stated that no more than 10 per cent of the anterior lobe could remain and still produce the changes typical of complete hypophysectomy. Thirty per cent of the gland apparently carried on its normal functions.

Growth and metabolism. Hypophysectomy produced the same general effects in all mammals. Each species, however, showed some differences. In all cases, growth was altered. Smith (1930) observed that in rats skeletal growth stopped very soon after the operation and that young animals remained infantile in appearance. If the animals were full grown when operated upon, cachexia appeared sooner. Collip, Selye and Thomson (1933) noted that growth continued for a time in young rats. There was a shrinkage and degeneration of the epiphyseal cartilages in young rats (Smith, 1930). The incisor teeth grew more slowly and there was a delay in

the eruption of the molars (Schour and Van Dyke, 1932). Gain in weight in puppies was due largely to deposition of fat (Benedict and Homans, 1912). There was a lower body temperature, pulse rate, respiratory rate and CO<sub>2</sub> production. Young rats remained infantile but older ones were unchanged in appearance. Richter and Wislocki (1930) stated that the spontaneous activity of hypophysectomized rats was reduced. Food intake and body weight were lower. Ascoli and Legnani (1912), Smith (1930), White (1933), McPhail (1935) and others reported that the heart, the liver and the spleen weighed less as compared to the body weight in animals with the gland totally removed. The fact that some animals became very fat while others grew thin often altered this finding. Smith (1930) caused adiposity to occur in rats by the injection of chromic acid by the temporal route. Many of the workers who used the temporal technique in hypophysectomy reported that adiposity occurred. Smith (1927) believed that the adiposity was caused by injury to the tuber cinereum. Aschner (1912) believed that death was caused in the dogs of Paulesco, Cushing and Homans, and Crowe, Cushing and Homans by injury to the tuber cinereum. In those cases, if they lived long enough, cachexia was produced. Dandy and Reichert (1925) stated that increased intracranial pressure might have been a factor in the deaths after temporal operations.

Blood sugar was lower in hypophysectomized than in normal dogs (Sachs and MacDonald, 1925, Koster and Geesink, 1929, Biasotti and Houssay, 1932, and D'Amour and Keller, 1933). In starving dogs it fell very low. Phillips and Robb (1934) reported the same thing in rats. Hypoglycemia might have been responsible for some of the deaths after hypophysectomy. Insulin

shock was produced with greater ease in hypophysectomized dogs (Houssay and Magenta, 1925, and others). McPhail (1935) stated that this was apparently not the case in ferrets.

Thyroid. The thyroid gland became inactive and atrophic after hypophysectomy (Aschner, 1912, Ascoli and Legnani, 1912, Dott, 1923, Smith, 1930, Houssay, Biasotti and Mazzocco, 1931, and McPhail, 1935). The follicular epithelium was flattened. The gland was smaller in size and the follicles were either larger or smaller. McPhail reported that there were small follicles with more interfollicular cells in the cat. White (1933) stated that in hypophysectomized rabbits the epithelium was flat.

Parathyroids. Baker (1942) reported a slight reduction in number and size of cells, but no change in cellular distribution or structure, in the monkey. Carnes, Osebold and Stoerk (1943) saw no impairment of the parathyroid in young male rats. Koster (1930) could find no degenerative changes in hypophysectomized dogs. The changes occurred in only about two-thirds of the cases in dogs (Houssay and Sammartino, 1933).

Adrenals. Atrophy of the adrenal cortex occurred after hypophysectomy in rats (Smith, 1930), in dogs (Ascoli and Legnani, 1912, and Houssay et al., 1933), in rabbits (White, 1933), and in mice (Gardner and Allen, 1942). The atrophy was found in the fascicular and reticular zones. Perla (1935) described hemorrhages in the reticular zone in the adult rat during the first two weeks after removal of the gland. Aschner (1912), on the other hand, reported an actual thickening of the cortex and an atrophy of the medulla.

Genital organs. All the workers have found regressive changes in the genital organs of adult animals and a lack of development in young animals

after hypophysectomy. Smith (1930) stated that in the rat regressive changes occurred in not only the germinal epithelium but also in the interstitial tissue of the testicle. Atrophy thus occurred in all of the accessory genitalia. Spermatogenesis ceased. Sexual desire was lost more quickly and more completely than after castration. Wiesner and Sheard (1933) also believed the latter to be the case. Spermatozoa survived for about three weeks after hypophysectomy in the rabbit (White 1932).

According to Smith (1930), the large and medium sized ovarian follicles including those continuing to develop from the reduced number of primordial follicles underwent atresia. Corpora lutea persisted for an abnormally long time. Swezy (1933) believed that the rate of ovogenesis was actually increased after hypophysectomy. Selye (1933) stated that both normal and atretic follicles were present in rats operated upon at 18 days of age and killed 10 to 25 days later. The theca cells about the atretic follicles appeared to be undergoing degeneration. Six months after removal of the pituitary in adult rats, the ovaries consisted mainly of cells of thecal origin. Estrus cycles did not occur. The uterus and vagina became atrophied in sexually mature animals and remained infantile in young animals.

Selye, Collip and Thomson (1933) and Pencharz and Long (1933) reported that in pregnant rats implantation was prevented if the gland was removed not more than 4 days after coitus. Death and resorption of the fetuses occurred if the operation was done between the 7th and 10th days. Between 11 and 20 days, hypophysectomy caused death of the mother or birth of dead or living young at the end of a prolonged period of gestation. The period

of gestation was prolonged from the normal of 21 to 22 days to 24 to 26 days. Parturition occurred in the absence of the pars neuralis even if the latter had been removed weeks before the termination of pregnancy (Smith, 1932). Pregnant rats operated upon 10 days before term lactated for a few hours after parturition. When lactating rats were hypophysectomized, lactation ceased in 24 hours. When the uterus was emptied in late pregnancy, lactation began in 36 hours but not if hypophysectomy had also been performed (Collip et al, 1933, and Jeffers, 1935).

Lactating mice also had no milk 24 hours after removal of the pituitary body (Selye, Collip and Thomson, 1933). The corpus luteum regressed rapidly in mice but persisted in rats. Hypophysectomy did not precipitate abortion as readily as did Oophorectomy in mice (Newton and Beck, 1939). Gardner and Allen (1942) reported that removal of the gland in mid-pregnancy in the mouse did not affect parturition. The corpus luteum was normal and the mammary gland developed. Lactation ceased on the second day. The interpubic ligament formed as in a normal animal at the time of parturition. No post-parturent mating occurred, however. Leblond and Nelson (1937), working with mice, believed that maternal instinct remains a nervous mechanism independent of pituitary hormones.

In pregnant guinea pigs hypophysectomized on the 34th to the 36th day of pregnancy, resorption of fetuses began within 2 days (Pencharz and Lyons, 1934). Those operated on the 40th to the 41st day carried on normal gestation. Only a slight and transient milk secretion occurred. The corpora lutea regressed rapidly.

Fee and Parkes (1929) showed that ovulation, which normally takes place about 10 hours after copulation in the rabbit, could be prevented by hypophysectomy performed within 1 hour after coitus. If the operation was performed after 1 hour, ovulation occurred and corpora lutea underwent normal but slower development (Deanesly, Fee and Parkes, 1930). The corpora lutea grew for 2 days but regressed after 4 days (Smith and White, 1931). Firor (1933) stated that hypophysectomy performed within 35 minutes after copulation prevented ovulation. If done between 50 minutes and 3 hours after copulation, it did not prevent ovulation but did prevent implantation. In rabbits operated upon in mid-pregnancy, there was fetal death. Normal termination of pregnancy occurred if the gland was not removed until the 24th to 26th day. White (1932) gave the time for prevention of ovulation as 1 hour. Operations in the 17 to 26 day period caused abortion. With those done in the 26 to 28 day period, living or dead young were born. No suckling or caring for the young occurred.

According to Hill and Parkes (1932), ovulation, which normally takes place in the ferret in 36 hours after copulation, could not be prevented if the operation was done more than 110 minutes after the beginning of mating. Ovulation which occurred following operations done soon after that time was not followed by corpus luteum development. Hypophysectomy of pregnant ferrets performed by the 21st day of gestation caused fetal absorption. If done on the 35th day, dead or living young were born in 3 to 8 days. Milk secretion rarely appeared and never persisted (McPhail, 1935).

Pregnant cats operated upon by Allan and Wiles (1932) gave birth to young normally in up to 11 days after the operation. They were obviously in

late pregnancy. McPhail (1935) stated that the removal of the gland from cats at mid-pregnancy caused abortion. Operations near the end of gestation did not influence parturition. No milk was secreted, however.

In hypophysectomized lactating goats, milk secretion ceased entirely. Only a temporary reduction in the amount of milk was found in partial removals (Hill et al. 1935).

Fig. Robinson (1937) completely hypophysectomized 4 suckling pigs by the intracranial route. They lived 1.5 to 3.5 months, perishing soon after weaning. He found a retardation of growth, especially in the long bones. The animals exhibited sporadic cramps. Their body temperature was 1 to 1.5 degrees below that of the controls. There was a lack of development of the gonads and thyroid, while the thymus completely atrophied. The adrenals were only slightly affected; in fact, the zona fasciculata seemed to exceed that of the controls. Extreme adiposity was noticed in some of the pigs which were only partially hypophysectomized.

## EXPERIMENTAL

### Materials and Methods

Seven male and four female pigs were hypophysectomized. They were allowed to live at least two months before they were destroyed by electrocution. The hypophysectomized and control pigs were housed and fed alike. The animals were weighed at the time of the operation and at the time they were electrocuted. The size, shape and the amount of adiposity present were noted. The endocrine glands and the heart, liver, spleen and kidneys were weighed (Table 3). Sections from the endocrine glands were fixed in Zenker-formol, 10 per cent formalin and Bouin's fluid and later imbedded in paraffin and sectioned at 8 microns. They were stained with Harris Hematoxylin and ethyl eosin. One male and one female control were used. The glands from two normal males and one normal female of the same age group were also used for comparison. X-ray pictures were taken of the leg and arm regions of the control and hypophysectomized pig to determine the growth of the long bones. All of the animals had been weaned but were sexually immature at operation time except one pregnant sow. The area of the pituitary fossa, including the bone and diencephalon, was removed at necropsy and fixed in 10 per cent formalin. The fossa was later examined for gland fragments. Any material hanging to the stalk or in the fossa was sectioned to be examined microscopically, unless the fragment of the gland was grossly detectable. In the latter case the animal was obviously only partially hypophysectomized.



Several very young pigs were used to study the relationship of the meninges to the pituitary. A portion of tissue, which included the gland, surrounding bone and membranes, and the adjacent portion of the brain, was removed from the head. It was fixed in 10 per cent formalin, decalcified in trichloroacetic acid, imbedded in paraffin and serially sectioned at 20 to 30 microns. They were stained with hematoxylin and eosin.

The gross structure of the pituitary gland and the surrounding area were studied. The arteries were injected with a thin aqueous suspension of red lead. The relative proportions of the various parts of the gland were determined by weight, and by measuring the parts in the serial sections.

The pituitary glands of five sexually immature pigs, three sexually mature females and two sexually mature males were removed at necropsy, fixed in Zenker-formol, imbedded in paraffin and serially sectioned at 6 microns. The sections were cut transversely to the long axis of the gland. One section from each of the areas 3, 4 and 5 (figure 3) was selected. The cells in 10 fields evenly distributed over the pars distalis of each section were counted. A binocular research microscope with a 4 millimeter objective and 15X oculars was used. Cross hairs in one of the oculars made the field easier to count. The microscopic structure of the various parts of the gland was observed in the serial sections. The pituitary glands of two barrows were prepared as above and examined for castration cells and structure in general. They were sectioned sagittally. The staining technique used for the sections examined for cells and microscopic structure was that of Koneff (1938) except that phosphomolybdic acid was used instead of phosphotungstic acid.

## Operative Techniques

### Parapharyngeal method

The animal is placed on its back on a trough-type operating table. Nembutal or 10 per cent chloral hydrate is given intravenously in the most prominent auricular vein until complete anesthesia is reached. The area from the body of the mandible to the sternum is shaved and disinfected. A liberal incision is made through the skin and subcutaneous tissue in the mid-line running through most of the distance from the mandible to the sternum. The larynx is exposed and held in position with one hand while a metal tracheal cannula is introduced through the mouth into the larynx and trachea. The muscles which run from the sternum to the larynx and hyoid bone are pushed aside and the operative area made deeper by blunt dissection. Care must be taken to remain medial to the structures in the carotid sheath and lateral to the trachea and esophagus. The posterior wall of the pharynx is pushed forward and is stripped from its attachment to the base of the skull as much as possible. An attempt is made to keep the pharyngeal wall intact, however. The insertions of the two ventral straight muscles on to the tuberosity at the sphenoid-occipital junction are thus exposed (figure XV). Laterally the bullae of the petrous temporal bones can be felt as large prominences. Between the bulla and the occipital and sphenoid bones at the area of the sphenoid-occipital junction is the foramen lacerum (figure I). Running through the medio-anterior portion of the foramen is the internal carotid artery. A trephine opening is made through the exposed portion of the sphenoid bone just anterior to the

insertions of the ventral straight muscles, and just posterior to the attachment of the pharyngeal wall to the sphenoid and vomer bones. For a 40-pound animal, a one-half inch trephine is used. The opening may be enlarged by means of a chisel if necessary. The bone is thicker anteriorly than posteriorly and in older animals may contain the sphenoidal sinus. The sphenoid bone in young animals is divided into the pre-sphenoid and post-sphenoid by a cartilaginous union (figure IV, 14). The cranial surface of the post-sphenoid contains the dorsum sellae (figures I, 2; II, 1; V, 3), which forms the posterior boundary of the pituitary fossa. The trephine opening should remove the bone forming the floor of the fossa in the area behind the optic groove. Since the intercavernous sinus containing the rete mirabile of the internal carotid artery is located just anterior to the base of the dorsum sellae (figure V, 4) the trephine opening should be kept as far anterior as possible to prevent opening of rete and possible resulting fatal hemorrhage. A certain amount of hemorrhage will occur at this point in the operation, however, and during the following manipulations. A long, five-sixteenths inch cannula like the one in the trachea with one end reduced in size to three-sixteenths inch and the other end attached to a suction hose is used to keep the area free of blood. Two short sharp needles project from the free end of the cannula to tear the dura from the ventral surface of the gland. The gland is sucked into the cannula piece by piece, or better, the whole gland is pulled loose at once by the suction contact with the cannula. After the dura has been torn, a cannula of the same size without needle prongs is used to remove the gland, which tears loose at the infundibulum. After the gland has been removed, the

bone opening is not filled but the skin is sutured.

Much care is taken in manipulating the cannula so as not to injure the diencephalon or mesencephalon in freeing the gland. Since the trephine opening is made as far anteriorly as possible to prevent hemorrhage, the mesencephalon is avoided. The gland lies in the anterior dorsal portion of the fossa and does not contact the sphenoid bone except in the anterior portion of the fossa (figure V, 2). Any injury to the brain stem will cause muscular rigidity and excitement, after which death occurs in a few hours. The source of negative pressure is provided by a motor driven adjustable pump (Boehnke rotary air blast and suction apparatus). A large bottle is inserted in the hose between the pump and the cannula to catch the blood and tissue fragments to prevent stoppage in the suction hose.

Temporal method ✓

The animal is placed on a trough-type operating table in the normal position. Nembutal is given intravenously in the ear vein until deep anesthesia is reached. The frontal, occipital and temporal areas are shaved, especially on the side to be operated, and disinfected. The head is turned so that one temporal area is upward. An incision is made through the skin antero-posteriorly in the center of the temporal fossa from the base of the ear to the supra-orbital area (figure XVI). The temporal fascia and muscle are incised to the bone. They are scraped from the bone of the fossa and laid downward as far as is permitted by the zygomatic arch. Some of the fascia and muscle is removed but enough must be left to be sutured over the bone opening later. The mouth is propped open to depress the

coronoid process of the mandible with its attached muscle and thus expose more of the bone in the temporal fossa. As large a trephine opening as space will permit is made through the bone in the floor of the fossa as far ventrally as possible. A three-fourths inch trephine is about the right size for a 40-pound pig. The opening can be enlarged by bone forceps if necessary. The dura mater is pierced and cut around the edge of the trephine opening, except ventro-laterally, where the flap is pushed to be replaced later (figure XVII). The head is turned to the side as much as will still allow the operator to view the opening from above. A curved spatula as wide as will go into the opening is introduced into the dural opening and the brain is pushed carefully toward the opposite side of the cranial cavity. The concavity of the spatula is in contact with the brain. As the pituitary area is approached, the subarachnoid cistern is punctured with the spatula to release the cerebrospinal fluid and allow more space for viewing the gland. The third cranial nerve is sighted, divided transversely by means of a probe, and pushed aside (figures VI, 3; VII, 3; XVIII, 3). Antero-medial to the nerve lies the internal carotid artery which must be avoided by staying posterior to it (figures VII, 2; XVIII, 1). With a thin probe which is slightly bent at the end but not sharp, the stalk is severed. The gland is then separated from the dura in the fossa by means of the probe. The attachment is firm posteriorly only. When the gland has been thoroughly loosened from the dural sac, it is removed by a small, slightly curved metal pipette and suction. It is removed in pieces or whole, if it can be lifted free by suction against the pipette. A hole in the side of the pipette allows the force of the suction to be regulated

by the operator's index finger. The size of the lumen of the pipette at its distal end is one-sixteenth to one-eighth inch in diameter. The fossa is explored for gland fragments. Throughout the process of exposing and removing the gland, cerebrospinal fluid and any blood that may appear are removed by the suction pipette. The dural flap is pushed back into place and the temporalis muscle and its fascia are sutured in their original position with cat gut after the mouth has been closed. The skin incision is closed by interrupted silk sutures. A collodian dressing is placed on the wound. Strict asepsis is maintained throughout the operation.

The instruments used in both operations are shown in figure XIV.

#### Observations

##### Constituents and relations of the hypophysis

The pituitary gland was attached by a slender stalk to the diencephalon just caudal to the optic chiasma. It lay in the hypophyseal fossa (sella turcica), (figure I, 3), which was a dural-lined depression in the dorsal surface of the sphenoid bone (figure II, 4). The hypophysis consisted of several divisions which may be classified either embryologically or anatomically. The portions derived from the oral epithelium were grouped together as the pars buccalis (pars glandularis, adeno-hypophysis), and the portion derived from the brain was called the pars nervosa (pars neuralis, neuro-hypophysis). The former included the pars distalis, pars tuberalis and pars intermedia. The pars distalis was separated from the pars intermedia and the pars nervosa by a cleft (residual lumen of Rathke's pouch). The

pars distalis was also called the anterior lobe and pars nervosa and pars intermedia together were designated as the posterior lobe.

The pars distalis was the largest division of the pituitary gland and surrounded the posterior lobe except dorsally and posteriorly (figure III, D). The pars nervosa was next in size and lay in the concavity of the pars distalis from which it was separated by the pars intermedia and the cleft (figure III, N). Its caudal or distal extremity protruded very slightly while its other extremity narrowed to a neck, the infundibulum, which was continuous with the diencephalon. A diverticulum of the third ventricle occupied the infundibulum near the diencephalon (figures IV, 2; XII, 1). The pars intermedia was joined to the periphery of the pars nervosa and was prominent in the area which was adjacent to the pars distalis, but was very thin or absent where the posterior lobe was not surrounded by the anterior lobe (figures III, I; IV, 6). Near the stalk it was continuous with the pars tuberalis which surrounded the infundibulum of the pars nervosa. The pars tuberalis was thick on the antero-ventral surface but thin on the opposite surface (figure III, T). The pars tuberalis capped the antero-dorsal portion of the pars distalis like an inverted cone and extended about half way down its anterior surface (figures III, T; IV, 5). It also had more contact with the brain on the anterior than on the posterior surface of the infundibulum. It was darker in color than the pars distalis. A line of black pigment sometimes demarked its upper portion from the diencephalon.

The pituitary gland in a 100-pound pig weighed about 180 mgs. Of this weight the pars distalis made up about 61 per cent, the pars neuralis about 25 per cent, the pars tuberalis and pars intermedia about 7 per

cent each. These percentages were determined by weighing the gland divisions and by measuring them in the serial sections.

The anterior and posterior lobes could be separated without difficulty except at the area of the pars tuberalis, which was fused with the pars distalis, the infundibulum and the pars intermedia. The gland lay in the pituitary fossa (sella turcica) with its long axis directed ventro-caudally (figure IV). The infundibulum joined the diencephalon antero-dorsally in relation to the gland. The anterior lobe was ventral and anterior in position, surrounding the posterior lobe except posteriorly and dorsally (figure III, D). The hypophysis possessed a thin capsule. The dura mater, which included the cranial periosteum, and the pituitary connective tissue were fused as one in the sella (figure IV, 8 and 9). The pituitary body could be easily separated from the dural sheath except at the caudal extremity of the posterior lobe where the attachment was firm. The dorsum sellae and its posterior clinoid processes were cartilaginous in young animals but became ossified to a greater extent with age. They were very prominent and formed the posterior wall of the fossa. The fossa was deeper posteriorly than anteriorly where it sloped upward to a shelf which was caudal to the optic groove (figures II, 2; IV). The gland did not contact the floor of the fossa except anteriorly. Posteriorly it contacted the dorsum sellae (figure V, 2). A periosteum lined the depth of the sella while a separate sheath of dura formed a support for the ventral portion of the gland (figures IV, 9). Dorsally the thick dura did not cover the gland except at the very posterior area and extended only slightly forward from the clinoid processes (figures IV, 8; VII, 4). A very thin transparent



sheath of dura often extended forward in contact with the pituitary from the thick dural termination for a short distance. As the neck was approached the subarachnoid space began (figure IV, 4). The pig thus has a very incomplete dural diaphragma sellae (figures IV, 8; VI, 4; VII, 4).

The area between the pituitary dura and the periosteum of the sellar floor formed a blood sinus (cavernous) which extended laterally and postero-ventrally to the gland joining the one on the other side (formed intercavernous sinus) (figures IV, 13; V, 4). A small blood sinus was also located on the posterior surface of the dorsum sellae (figure II, 2; IV, 12). The main dural sinus contained a complex capillary-size arterial network (rete mirabile) formed by the two internal carotid arteries as they entered the lateral areas of the fossa. The networks formed by the right and left arteries connected in the sinus in a plexiform manner. Small inferior hypophyseal arteries arose from this to enter the posterior lobe and cleft area. The internal carotid artery on each side left the plexus and perforated the dura to enter the anterior part of the fossa just lateral to the stalk and posterior to the optic groove (figure VII, 2). The third cranial nerve coursed downward and forward to enter the foramen orbito-rotundum lateral to the internal carotid artery (figure VII, 3). The internal carotid artery entered the subarachnoid space where it gave off a posterior communicating artery and continued on anteriorly. These entered into the formation of the arterial circle (Circulus arteriosus of Willis) (figure VIII). Several small superior hypophyseal arteries arose from the internal carotid and posterior communicating arteries to supply the infundibular stalk, pars tuberalis, pars distalis and slightly the

posterior lobe. Veins left the posterior pole, where it was adherent to the dura, to enter the intercavernous portion of the dural blood sinus. Small veins coursed from the areas supplied by the superior hypophyseal arteries to enter the cavernous sinuses directly.

#### Microscopic structure

The divisions of the hypophysis cerebri changed in size and shape in relation to each other at different levels in the gland. If the gland were sectioned transversely to its long axis, those relations could be seen (figure III). At level 5, the pars nervosa reached its largest size. This diminished to level 2 where it enlarged slightly to become hollow at level 1 to join the brain. The pars distalis was largest at level 3 or the center of the gland. It was in general U-shaped throughout. The pars intermedia was present where the pars nervosa lay in the concavity of the pars distalis. It was very thin or absent elsewhere except at level 2 where it surrounded the neural tube and became continuous with the pars tuberalis. Its union with the nervosa formed only a slightly irregular line. It was separated from the pars distalis by the residual lumen of Rathke's pouch except at the dorsal areas where the posterior lobe came into view. Here it spread out into the pars distalis on each side. The invasion of the pars distalis by the pars intermedia was greatest at levels 2 and 3 and slight at 5. The residual cleft became increasingly smaller from levels 5 to 2. The pars tuberalis capped the anterior area of the pars distalis and extended about half way down its anterior surface. It surrounded the infundibular stalk but was thin posteriorly. It was more

extensive in its termination at the tuber cinereum anteriorly. The ventral tip of the pars tuberalis showed at level 2(T). Its appearance was darker than that of the pars distalis. The cone of Wulzen (1914) was not seen.

Pars distalis. Three types of cells were recognized: (1) basophils (cyanophils, beta cells); (2) acidophils (eosinophils, oxyphils, alpha cells); (3) chromophobes (reserve cells, neutrophils, chief cells) (figures IX, X). The basophils were usually the largest of the cells, although some small basophils were present. The cytoplasm stained blue with Mallory's or Koneff's stains. Some were dark blue while others were light blue. Their shape was usually round or oval. The cytoplasm contained fine granules. Occasionally a clear area (macula) was seen near the nucleus. The nucleus was round or oval and slightly vesicular with dark staining chromatin. Parachromatin was often seen in the nuclei. Some of the dark cells had small pyknotic nuclei which were red in color. The acidophils were usually smaller and more angular than the basophils. The cytoplasm contained large red staining granules, which stained more acidophilic in some cells than in others. The nuclei were similar to those of the basophils. The chromophobes were the smallest of the cells although some were large. Often the cytoplasm was so pale that only the nucleus could be seen. The cytoplasm frequently stained slightly basophilic but might even be slightly acidophilic. The nuclei did not differ from those of the other cells.

The cells of the pars distalis were arranged in closely packed groups which were separated from each other by a small amount of connective tissue. The chromophobes often occupied a position nearer the center of the cell cords. Blood sinusoids were numerous and some of them contained

colloid. They were separated from the cells by connective tissue. All cell types were found throughout the pars distalis. The acidophils were not as numerous near the midline or center of the lobe (except near the cleft) and very few were found near the pars tuberalis. They were more numerous in the lateral and distal or posterior areas. The chromophobes were evenly distributed while the basophils were more numerous in the acidophil-scarce areas (figure III,a). Slightly basophilic cuboidal to columnar cells were frequently found in the pars distalis bounding the cleft.

Pars intermedia. The cells were arranged in cords and were slightly basophilic. Sinusoids and vesicles containing colloid and cellular debris were numerous (figure XI, I).

Pars tuberalis. The cells were arranged in irregular groups or even acini with intervening connective tissue. They were chromophobic or slightly basophilic. Sinusoids and colloid vesicles were numerous. It was difficult to determine where the pars tuberalis joined the pars intermedia (figures XII, 3; XIII).

Pars nervosa. Many radiating capillaries were present. Nerve strands and glia cells (pituicytes) made up the bulk of the lobe. Some small hyalin or colloid deposits could be detected (figure XI, N).

Cell counts. The cell counts of the pars distalis are shown in table 2. Only those with nuclei were included. More acidophils were found at level 5 than at 4 or 3; more basophils were found at level 3 than at 4 or 5 (figure III). The percentages were; sexually immature pigs A-38.6, B-11.5,

C-49.9; sexually mature diestrus females A-53.1, B-10.6, C-36.3; sexually mature males A-57.4, B-10.7, C-31.9.

#### Effects of hypophysectomy

The weights of the glands and organs of the hypophysectomized, partially hypophysectomized and control pigs are shown in Table III. Of the eleven operated animals that lived, five were considered to be hypophysectomized. By microscopic examination of any material in the fossa and at the infundibular area only a few cells were found in those labeled completely hypophysectomized. In the latter group the cells remaining were estimated to be less than 10 per cent of the pars distalis.

In the following discussion, "S" stands for female and "B" for male. Animals S1, S2, B1, B2 and B3 were considered to be hypophysectomized. Animals S3, S4, B4, B5, B6 and B7 were partially hypophysectomized.

Animal S1 was operated upon by the parapharyngeal method. In all the others the temporal method was used. Considerable connective tissue surrounding a small nest of cells was found attached to the remnant of the stalk of the hypophysis in animal S1. Eighty-one days after the operation she farrowed 7 pigs. They appeared to be normal but by the next day all were dead. She exhibited no motherly instinct and had very little mammary gland development and no milk secretion. Up to 174 days after the operation, when she was killed, no signs of estrus had appeared. Although she weighed more than 200 pounds, her ovaries were actually smaller than those of the 100-pound control for the other group. No corpora lutea were present although several corpora albicantes could be seen. The larger follicles were

becoming atretic. There were some cell nests and small follicles with ova. Much connective tissue was present (figure XXIV). The thyroid follicles were of medium size and the epithelium was of medium height. The adrenal glands appeared to be normal.

Animal S2, killed 86 days after the operation, had a few cells attached to the stalk. She showed some growth in height but didn't become any fatter than the control. The whole genital system showed a lack of development. The ovaries (figure XXIII) were very small in comparison to those of the control and only cell nests and small follicles were present in the cortical area (figure XXV). The uterus was small and the glands were few (figures XXVII, XXVIII). The vaginal epithelium was much narrower than in the control (figures XXIX, XXX). The thyroid follicles were small and the epithelium was low cuboidal in type (figures XLI, XLII). The adrenals appeared to be normal.

Animal B1 was completely hypophysectomized but died, for no reason which was determined, 17 days after the operation. He had gained one pound. The genital apparatus was undeveloped, but the pig weighed only 47 pounds, so the genital organs probably would not have been much larger. The thyroid follicles were small and the epithelium low in height.

Animal B2, killed 82 days after the operation, showed only a few cells attached to the stalk. The animal became very fat and showed very little growth of the long bones (figures XXI, XXII). The thyroid follicles were large and filled with colloid and the epithelium was very flat in type (figures XL, XLII). The adrenal glands seemed normal. The animal had been castrated some time before the operation.

Animal B3, killed 89 days after the operation, had a very small cellular spicule attached to the remnant of the hypophyseal stalk. Growth was slight and the animal remained squatty and became very fat (figures XIX, XX). The thyroid follicles were large and filled with colloid and the epithelium was low cuboidal in type (figures XL, XLII). The thyroid picture was identical with that of B2. The adrenal glands showed a reduction in size of the cortex except the glomerular zone (figures XLIII, XLIV). The genitalia developed only slightly. The testicles were small and the cells had developed only to the spermatocyte stage (figures XXXI, XXXII). Some of the tubule cells were pyknotic and the interstitial cells were few in number. The prostate, seminal vesicles and bulbo-urethral glands (figures XXXIV to XXXIX) showed only slight glandular development. The accessory genitalia weighed even less than those of animal B1.

In the other animals, definite pieces of the anterior lobe were found at necropsy. No gland fragment was estimated to be greater in size than one-third of the anterior lobe. Growth, appearance, gland weights, and glandular structure in animals B4, B5 and S3 were like those of the controls. B6 and B7 had small adrenal glands. The adrenals, however, did not exhibit cortical atrophy. There were many interstitial cells in the testicles of animal B7 (figure XXXIII). Animal S4 did not grow much in height and became very fat. Her glands appeared to be normal histologically.

Definite atrophy of the thymus was not seen in any of the animals. The differences in the state of adiposity in the various animals made it difficult to compare gland or organ size to body weight.

## DISCUSSION

### Anatomical

This is a preliminary investigation of the structure and functions of the porcine hypophysis. Much time has been spent in establishing the normal structure and relations. Some of the physiological aspects will need to be investigated further.

The meningeal relations described by Wislocki (1937) for man, the rat, the rabbit, the cat, the dog, and the monkey are also found in the pig. However, the gland does not contact the floor of the deep hypophyseal fossa except anteriorly. The area between the dura adjacent to the gland and the periosteum of the fossa forms a large blood sinus in which is found the rete mirabile of the internal carotid arteries. Hill et al (1935) encountered a similar plexus in the goat. Sisson and Grossman (1938) described a large rete mirabile in the ox. The incomplete diaphragma sellae makes the gland easily visible from the cranial cavity in the pig. The arrangement of the arteries into two sets, superior and inferior hypophyseal arteries, is found in the pig. It follows the description by Wislocki (1937) for the cat, the monkey and man. The drainage of the sinusoids of the anterior lobe into a venous circle which lies as a satellite to the arterial circle in the dog (Dandy and Goetsch, 1911, and Basir, 1932) was not found. They drain directly into the cavernous sinus. The portal veins will need to be investigated as will also the nerve supply to the gland.

The classification of the different parts of the pituitary body used by Tilney and Riley (1938) and by Rasmussen (1939) is preferred. The



pars glandularis is the same as the pars buccalis and designates the portions arising from Rathke's pouch. The anterior lobe is called the pars distalis by them.

The 6 to 9 types of cells described by Warbritton and McKenzie (1937) in ewes probably represent cells in different stages of secretion. Wolfe, Cleveland and Campbell (1933) found two types of basophils as to granules in the dog. Cleveland and Wolfe (1933) observed granule variation in the cells, especially the basophils, in the sow's pituitary. In this investigation, although the cells in each group show differences in staining properties and granulation, the three fundamental classifications have been retained. Severinghaus (1938) questioned the assumption that a cell full of granules is necessarily very active. He stated that a cell might be so active that its secretion granules are all discharged in the process of rapid secretion. It would thus appear as one which is devoid of granules and apparently inactive.

Rasmussen (1939) and others have shown that the cell numbers vary much in different individuals. The range of chromophobes in man was 33 to 37 per cent, the acidophils 19 to 59 per cent, and the basophils from 5 to 27 per cent. This makes it imperative that large numbers of cells be counted. More cell counts will be made especially to determine cyclic variations in the sow.

It is generally believed that the chromophobes are the stem cells and that they become basophils or acidophils. In active secretion the process can be reversed (Severinghaus, 1937). As the animal grows the chromophobes should tend to decrease slightly and the chromophils increase.

This has usually been the case. Nelson (1933) believed that in the pig the basophils influence growth and the acidophils influence the gonads. This is the opposite of the usual conclusions for other animals. Cleveland and Wolfe (1933) found most of the cellular variation as to granules during the estrus cycle in sows to be in the basophils, although the acidophils were altered. The present work on the pig shows the basophil count to be constant and less than the other cell types as is the case in other animals. Severinghaus (1937) has proposed a cycle of ovary-pituitary relationship for man. Estrone stimulates the basophils which influence the ovarian follicles to produce estrone. An excess of estrone stimulates the acidophils to influence the growth of the corpus luteum, which in turn produces progesterone. Progesterone in excess stimulates the basophils. It appears from the above discussion that both the acidophils and basophils influence the gonads. This is probably true in the pig as well as in other animals.

As was found by Rasmussen (1939) in man, Kirkman (1937) in the guinea pig, Smith and Smith (1923) and Spaul and Howes (1930) in the ox, and Nelson (1933) in the fetal pig, the basophils are more numerous in the central areas than elsewhere and the acidophils are more numerous in the lateral areas. Nukarya (1926), however, found the reverse to be the case in the rat. Basophils are numerous and acidophils scarce in the area adjacent to the pars tuberalis. This was also noted by Kirkman (1937). Dawson (1937) described this area in the cat and rabbit, where he stated that it was composed of basophils and chromophobes, and called it the zona tuberalis. It is almost missed in counts at level 3. If counts were made

in the area capped by the pars tuberalis the basophil total might be slightly higher. Cleveland and Wolfe (1933) found almost as many basophils as other types in the pars distalis. Perhaps they included more of the slightly basophilic cells into the basophil group, while in this investigation more of them were placed in the chromophobe group. Kirkman (1937) placed some of the light basophilic cells in the chromophobe count.

Chromophobes were found to be the most numerous cell type in man (Rasmussen, 1939), and in rats (Wolfe and Cleveland, 1933). Acidophils were the most numerous type in the guinea pig (Kirkman, 1937), in the dog (Wolfe, Cleveland and Campbell, 1933), and in the pig (Cleveland and Wolfe, 1933). In this investigation the chromophobes were found to be most numerous in immature pigs and acidophils in sexually mature pigs. Cleveland and Wolfe (1933) observed an increase in acidophils and a decrease in chromophobes in sexually mature over sexually immature pigs.

Castration changes that have been described by many in the rat were not seen in the pig. Severinghaus (1932) did not find them in the guinea pig.

The method developed by Rasmussen and Herrick (1922) for counting cells has generally been used by investigators. The glands were serially sectioned horizontally and sections one-fourth, one-half and three-fourths of the way through the gland were used. They counted every 5th field. Cleveland and Wolfe (1933) obtained uniform results when every 10th or even every 25th field was counted. In this work the glands were cut and

the sections selected in the same manner but 10 fields evenly distributed to cover that section of the lobe were counted.

### Hypophysectomy /

The number of animals not surviving the operation is great. Many factors contribute to the high death rate. The arterial plexus and dural sinuses in the pituitary fossa ventral and posterior to the gland cause much hemorrhage when not avoided in the parapharyngeal approach. The diencephalon and mesencephalon are more apt to be injured in removing the gland ventrally since the diaphragma sellae is incomplete. Injury to the brain in this area results in muscular rigidity and excitement, which cause death in a few hours. Complete removal of the gland without brain injury or too much hemorrhage is difficult to achieve from this approach. Hill et al (1935) avoided plexus hemorrhage and brain injury by using a high frequency electric current to remove the gland and to cauterize the vessels. By not entering the pharynx, the danger of infection is reduced. The operative area being ventral allows for good drainage of blood and exudates. Anesthesia does not need to be carried to a state of complete relaxation.

By the temporal method, the entire gland can be removed with less danger of hemorrhage or brain injury. Slight injury to the cerebrum in pushing the brain to one side is not harmful. It was found that shrinking the brain by the intravenous injection of a hypertonic salt solution, as proposed by Weed and McKibbin (1919) is not necessary. The third cranial

nerve is always severed and pushed aside to allow the gland to be seen clearly. The lateral turning of the one eye doesn't seem to disturb the animal or its vision. The small internal carotid artery must be avoided. Suction works very well in removing cerebrospinal fluid, blood and the loosened gland. Some of the animals died in 24 to 48 hours in extreme depression. This has been ascribed to tuber cinereum injury (Aschner, 1912). Maybe it is a syndrome of hypoglycemia (Biasotti and Houssay, 1932, and D'Amour and Keller, 1933). Increased intracranial pressure might be a factor. Aseptic precautions must be taken; however, infection seldom occurred. Since anesthesia must be very deep in intracranial operations, large pigs seldom survived. An attempt should be made to bring the large animals out of the influence of the anesthetic very rapidly. Deep anesthesia may affect the fetuses of pregnant animals. For successful recoveries after hypophysectomy, the animals must be able to move about and to take food and water a few hours after the operation. No attempt was made to supply pituitary hormones to help the animals over the post operative period. If the animal readily eats and drinks, recovery is expected.

Since the animals were kept inside on cement throughout the observation period, vitamin D was supplied to the ration. The animals were not fed for rapid gains, however. The controls did not show the gains which should be expected although growth of skeleton and organs was normal. Perhaps in future experiments the animals should be kept outside. No operations were done in winter. ✓

Aschner (1912) considered his dogs to be completely hypophysectomized if no glandular tissue could be found grossly. Smith (1932) believed that in rats no more than 10 per cent of the anterior lobe could remain if the removal was to be considered total. He found that 30 per cent of the gland was enough to maintain normal functions. From these experiments with pigs, small cellular remnants were found to support certain normal functions. The pars distalis is either not necessary to maintain pregnancy after the first month in the sow or pregnancy can continue when only a very few anterior lobe cells are present. More pregnant sows must be hypophysectomized to determine this point. Milk apparently is not secreted even though pregnancy has been maintained. Leblond and Nelson (1937) believed that maternal instinct in mice remains a nervous mechanism independent of pituitary hormones. White (1932), however, found that the hypophysectomized rabbits did not care for their young. The hypophysectomized sow in these experiments showed no maternal instinct. Hypophyseal deficiency apparently influences the gonads and thyroid gland more readily than it does the adrenals.

The fact that some animals become very fat while others do not makes it difficult to compare organ weight to body weight. In those with much adipose tissue the thyroid follicles are very large and filled with colloid as in ordinary hypothyroidism. Thyroids of this type are not smaller in weight than normal. The animal's gain in weight is due to excess fat rather than to growth. The X-ray pictures show the comparison of length of long bones in normal and operated animals, but since the growing period

had not ceased, very little difference can be seen in the epiphyseal cartilage regions.

Robinson (1937) found the adrenals to be only slightly affected in hypophysectomized suckling pigs. More work should be done in regard to the adrenal. Atrophy of the cortex apparently does not always occur. The thymus needs further observations. The parathyroid glands which are difficult to locate in the pig should be investigated. Schlotthauer and Higgins (1934) stated that the parathyroids are usually found in the anterior portion of the thymus. The fact that the pig puts on much fat so readily makes the study of metabolic effects of hypophysectomy advisable. Hormone replacement therapy will add to the knowledge of pituitary functions. The stalk may be cut to investigate the posterior lobe.

Kingsbury (1942) considered the pharyngeal hypophysis, which is found often in man and the dog, functionally unimportant. Nelson (1933) did not find it in fetal pigs. Even if it is present in the pig, it probably has no significance.

Whereas Phillips and Zeller (1943) stated that estrus did not occur until the animals were about 200 days old and about 190 pounds in weight, corpora albicantes were seen in the ovaries of the 100-pound control pig used in these experiments. She, however, was at least five months of age.

### SUMMARY AND CONCLUSIONS

1. The hypophysis cerebri of the pig consists of the pars distalis, pars tuberalis, pars intermedia and pars nervosa. The pars intermedia and pars nervosa together form the posterior lobe which is separated from the anterior lobe by the residual lumen of Rathke's pouch. The anterior lobe is formed by the pars distalis, although a portion of the pars tuberalis is often included in it.

2. The pars distalis makes up about 61 per cent of the gland. It is antero-ventral in position and surrounds the posterior lobe except posteriorly and dorsally. Its cells occur in closely packed groups separated from other groups by a small amount of connective tissue. Three types of cells are recognized: basophils, acidophils and chromophobes. The basophils are the least numerous, averaging about 11 per cent. They are usually the largest although some are smaller, and are round to oval in shape. The cytoplasm is basophilic in staining properties and usually contains small granules. Some cells appear dark blue with Koneff's or Mallory's stains while others are light blue. The nuclei of all three major types of cells in the pars distalis are similar in appearance, being round to oval and vesicular with dark chromatin. Some of the nuclei in the basophils are small and acidophilic. The acidophils are usually smaller and irregularly oval and angular in shape. They average about 39 per cent in number in sexually immature pigs, 53 per cent in sexually mature females, and 57 per cent in sexually mature males. The granules are larger than those of the basophils and are acidophilic, although some



stain more deeply than others. Their size also is not constant, yet more so than the basophils. The cytoplasm of the chromophobes usually stains slightly basophilic but may be so pale that only the nuclei can be recognized. Some chromophobes stain very slightly acidophilic. They vary in size and shape. About 50 per cent of the cells in sexually immature animals are chromophobes. In sexually mature females they average about 36 per cent and in sexually mature males about 32 per cent. All cell types are found throughout the pars distalis. The central area except near the cleft is acidophil-poor and basophil-rich as especially is the area next to the pars tuberalis. The acidophils are found more in the lateral and distal portions of the lobe whereas the chromophobes are evenly distributed. Mitoses are rarely seen. Many blood sinusoids and some colloid are present. "Castration" cells were not found.

3. The pars tuberalis makes up about 7 per cent of the pituitary gland. Its cells are arranged in irregular groups or even acini with intervening connective tissue and are chromophobic or slightly basophilic. Sinusoids and colloid vesicles are numerous. The pars tuberalis is extensive in the pig and caps the anterior portion of the pars distalis and extends along the infundibular stalk to the brain. It surrounds the infundibular portion being most extensive anteriorly. Distally it is continuous with the pars intermedia.

4. The pars intermedia surrounds the pars nervosa except dorsally and posteriorly where it is thin or absent. Where it appears dorsally from the concavity of the pars distalis, it spreads out slightly into the pars distalis. Its volume is about 7 per cent of the gland. The

cells are arranged in cords and are slightly basophilic. Sinusoids and vesicles containing colloid and cellular debris are numerous.

5. The pars nervosa occupies about 25 per cent of the gland and lies with the pars intermedia in the cavity of the pars distalis. The enlarged distal end projects slightly from the anterior lobe; the narrow neck or infundibulum is continuous with the tuber cinereum. The neck contains a diverticulum of the third ventricle. Many radiating capillaries are present throughout. Nerve fibers and glia cells make up the bulk of the lobe and small hyalin or colloid deposits are often present.

6. The pituitary gland lies in the upper part of the pituitary fossa or sella turcica with the infundibular area dorso-anterior and the distal portion posterior. The gland capsule and the duro-periosteal sheath are adherent to each other but can be easily separated except at the caudal extremity of the posterior lobe. The subdural and subarachnoid spaces are not present around the gland except at and slightly posterior to the stalk. The dural diaphragma sellae is very incomplete since the thick dura extends only slightly forward from the posterior clinoid processes. The dura which contacts the gland ventrally is separated from the periosteum which lines the fossa. The pituitary body contacts the bone only anteriorly in the fossa and at the posterior clinoid area (usually cartilaginous).

7. The blood supply comes by way of the superior hypophyseal arteries from the internal carotid and posterior communicating arteries, and the inferior hypophyseal arteries arise from the rete mirabile in the intercavernous sinus. The former supply the stalk, pars tuberalis

and pars distalis; the latter go to the posterior or distal pole of the gland. Blood returns from the stalk, pars distalis and pars tuberalis to the cavernous sinuses, and from the posterior lobe to the intercavernous sinus where the gland and dura adhere to each other. The cavernous and intercavernous sinuses occupy the area between the dura which is in contact with the gland, and the periosteum of the fossa. The rete mirabile of the internal carotid arteries is in these sinuses.

8. Eleven pigs were hypophysectomized, of which five were considered as having the gland completely removed. A parapharyngeal and a temporal method of removing the pituitary gland from living pigs were developed. The temporal method proved to be the better of the two.

9. If more than a few anterior lobe cells remain, all of the effects of complete hypophysectomy are not seen. If the portion remaining can be detected, few or no effects of deficiency are found.

10. Growth is inhibited when the anterior lobe is absent. The animals may become very fat. Lack of growth is most noticeable in the long bones.

11. After hypophysectomy the cells of the seminiferous tubules of the testicle in sexually immature animals do not develop into spermatazoa and the testicles remain small in size. The interstitial cells are also affected as is shown by the lack of development of the accessory genital organs. The connective tissue septa are more extensive than the glandular portions of the prostate, seminal vesicles and bulbo-urethral glands.

12. The ovaries in immature hypophysectomized females remain small and large follicles do not develop. In mature females the large follicles become atretic and estrus does not occur. Any corpora lutea present at

the time of pituitary removal regress rapidly. Milk cannot be secreted. Apparently very few anterior lobe cells are necessary to maintain pregnancy but more are necessary to cause milk secretion. Parturition appears to occur normally without the presence of the posterior lobe. After hypophysectomy in the immature female, the uterine glands remain few in number and the vaginal epithelium stays thin.

13. In the hypophysectomized animals the thyroid epithelium is low cuboidal in type. The follicles may be small with much interfollicular tissue or they may be large and distended with colloid. The latter type is found in the animals that become very fat. The size and weight of the gland is influenced by the size of the follicles and the amount of colloid.

14. The adrenal glands apparently do not always show signs of pituitary deficiency. If cortical atrophy is present, the glomerular zone is not involved.

15. Definite atrophy of the thymus was not seen after hypophysectomy.

16. More of the anterior lobe must be present to maintain some functions than others. The effects of hypophysectomy considered here are due to the absence of the anterior lobe.

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Figure I

Hypophyseal fossa. Dorsal view.

1. Foramen lacerum.
2. Dorsum sellae.
3. Hypophyseal fossa (Sella turcica).
4. Optic groove.

Figure II

Hypophyseal fossa. Lateral view.

1. Dorsum sellae with posterior clinoid processes.
2. Blood sinus.
3. Floor of hypophyseal fossa.
4. Area of fossa occupied by dural blood sinus.
5. Flap of dura which encloses the pituitary body.





Figure I

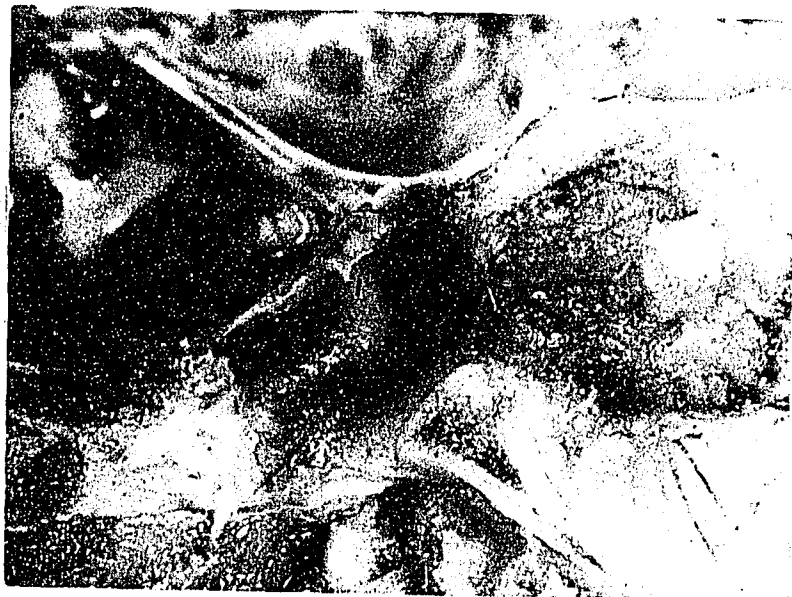


Figure II

Figure III

Crosssections of the pituitary gland.

Levels are numbered.

- T. Pars tuberalis.
- D. Pars distalis.
- N. Pars nervosa.
- I. Pars intermedia.
- R. Residual cleft of Rathle's pouch.
- V. Diverticulum of third ventricle.
- a. Basophil area.
- b. Sinusoids.

Figure III

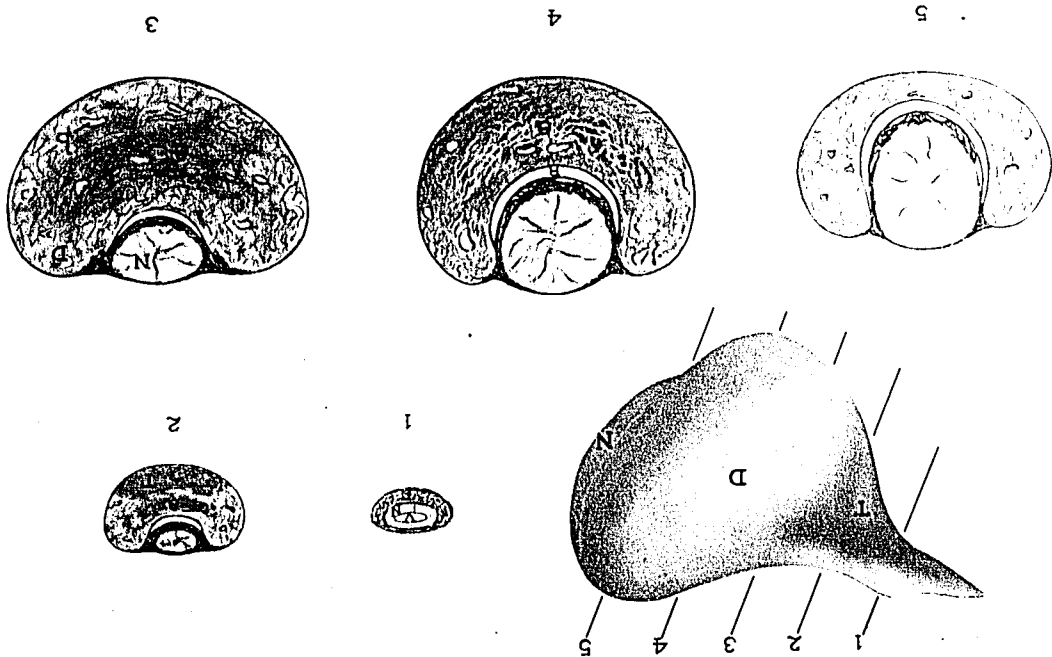


Figure IV

Meningeal relationship. Sagittal view.

1. Brain.
2. Third ventricle.
3. Pars nervosa.
4. Subarachnoid space.
5. Pars tuberalis.
6. Pars intermedia.
7. Pars distalis.
8. Anterior limit of the thick dural diaphragma sellae.
9. Dura of gland.
10. Dorsum sellae (cartilagenous).
11. Dorsum sellae (osseous).
12. Small blood sinus.
13. Area of fossa containing blood sinus.
14. Cartilagenous union between presphenoid and postsphenoid.
15. Sphenoid bone.

Figure V

Sagittal view of cranial cavity and brain.

1. Optic chiasma.
2. Hypophysis cerebri.
3. Dorsum sellae.

Figure V (continued)

4. Blood sinus and rete mirabile.
5. Sphenoid bone.
6. Anterior wall of pharynx.
7. Ventral straight muscles.



Figure IV



Figure V

Figure VI

Fossa with gland removed. Dorsal view.

1. Optic chiasma.
2. Hypophyseal fossa with dura intact.
3. Oculomotor nerve.
4. Dorsum sellae.

Figure VII

Fossa with gland intact. Dorsal view.

1. Optic chiasma.
2. Internal carotid artery.
3. Oculomotor nerve.
4. Dorsum sellae.
5. Pars distalis.
6. Pars nervosa.

Figure VIII

Circle of Willis. Dorsal view.

1. Optic chiasma.
2. Anterior cerebral artery.
3. Basilar artery.
4. Middle cerebral artery.
5. Posterior communicating artery.



Figure VI



Figure VII



Figure VIII



Figure IX

Cells of pars distalis. Drawing.

1. Chromophobe (basophilic).
2. Chromophobe.
3. Chromophobe (acidophilic).
4. Acidophil.
5. Basophil (light).
6. Sinusoid.
7. Colloid.
8. Basophil (dark).

Figure X

Section of the pars distalis showing cell types. Koneff's stain  
800X.

1. Basophil (dark).
2. Basophil (light).
3. Acidophil.
4. Chromophobe.
5. Sinusoid.



Figure IX

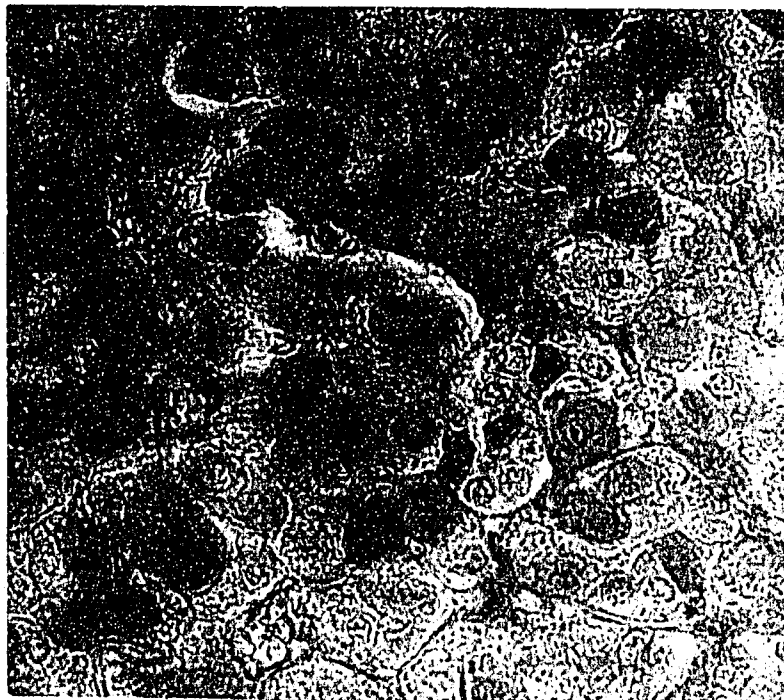


Figure X

Figure XI

Section of the pars intermedia and pars nervosa. Hematoxylin-eosin.  
400X.

- I. Pars intermedia.
- N. Pars nervosa.
- 1. Sinusoid with colloid.
- 2. Capillary.
- 3. Colloid.
- 4. Sinusoid.

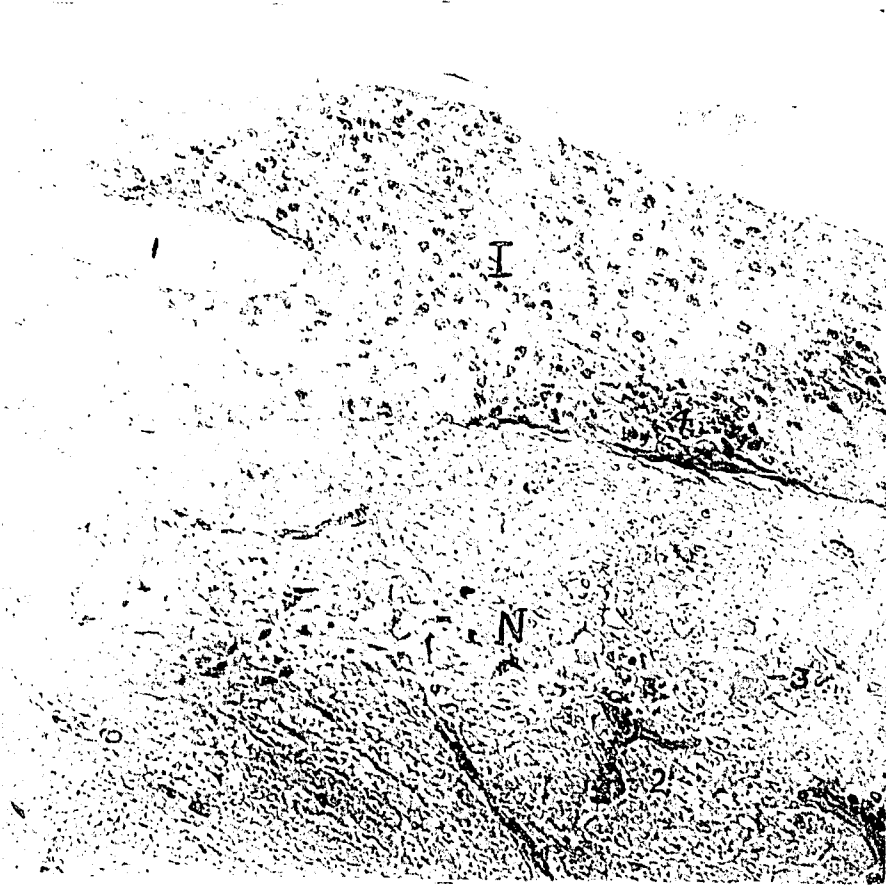


Figure XI

Figure XII

Section of the region of the pars tuberalis. Koneff's stain.

30X.

1. Diverticulum of third ventricle.
2. Pars nervosa.
3. Pars tuberalis.
4. Pars distalis. \*
5. Pars intermedia.

Figure XIII

Section of the pars tuberalis. Koneff's stain. 800X.

1. Sinusoid.

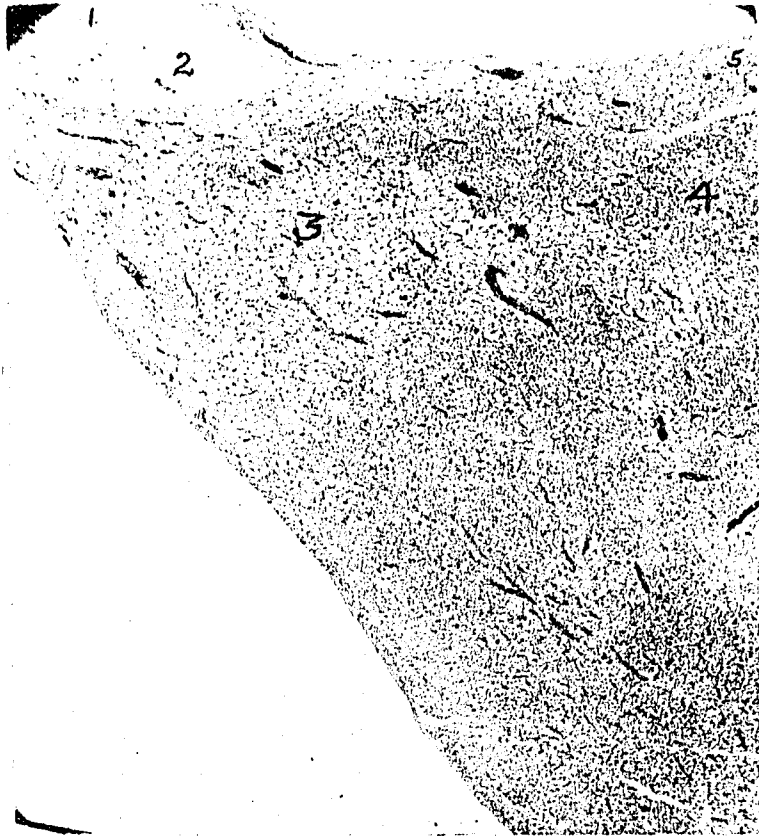


Figure XII

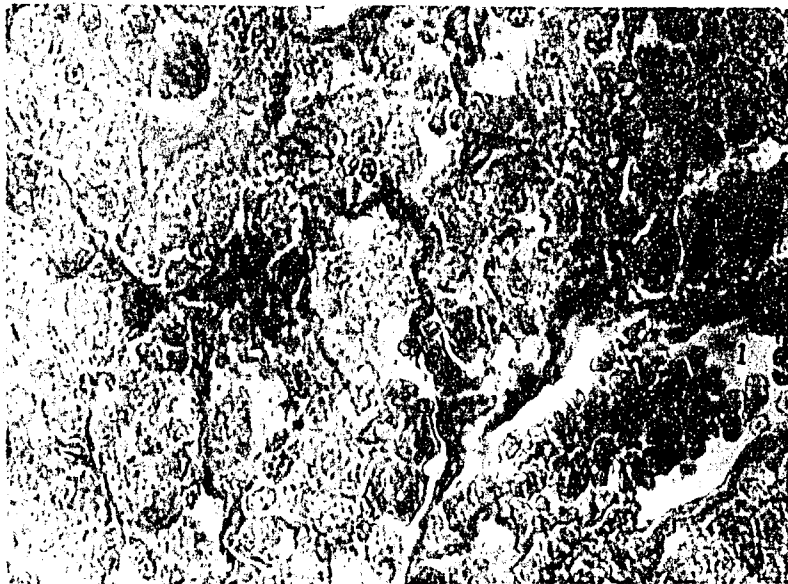


Figure XIII

Figure XIV

Surgical instruments.

Figure XV

Ventral view of operative sight, parapharyngeal method.

1. Wall of pharynx.
2. Ventral straight muscles.

Figure XVI

Area of incision for the temporal operation.

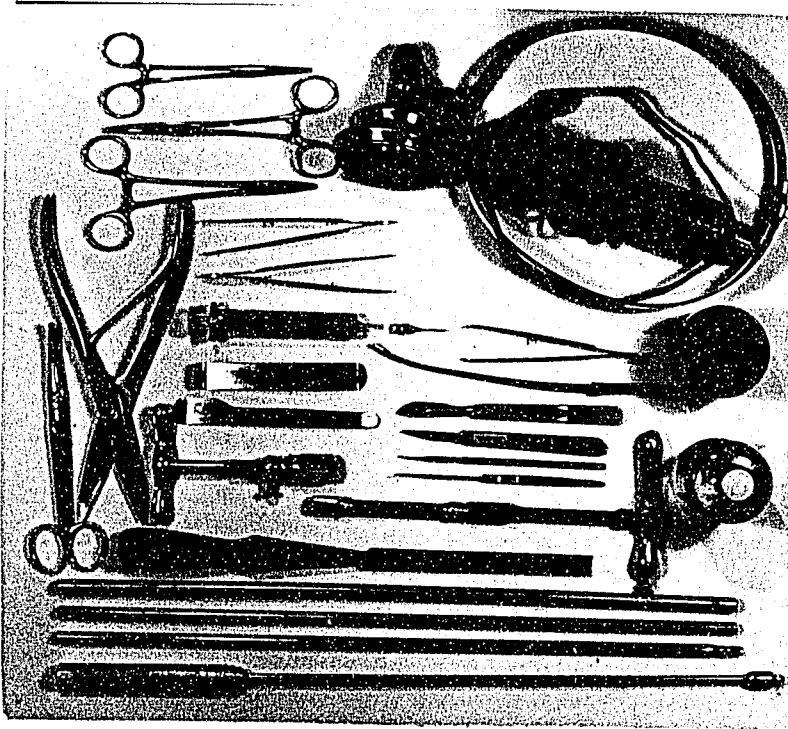


Figure XIV



Figure XV



Figure XVI



Figure XVII

Opening into cranial cavity for the temporal operation.

Figure XVIII

Pituitary gland and surrounding structures as seen in the  
temporal operation.

1. Internal carotid artery.
2. Pituitary gland
3. Oculomotor nerve.
4. Optic chiasma



Figure XVII



Figure XVIII

Figure XIX

Control animal, left; hypophysectomized animal, right.

Figure XX

Control animal, left; hypophysectomized animal, right.



Figure XIX



Figure XX

Figure XXI

X-ray of tibia and fibula of hypophysectomized pig.

Figure XXII

X-ray of tibia and fibula of control.



Figure XXI

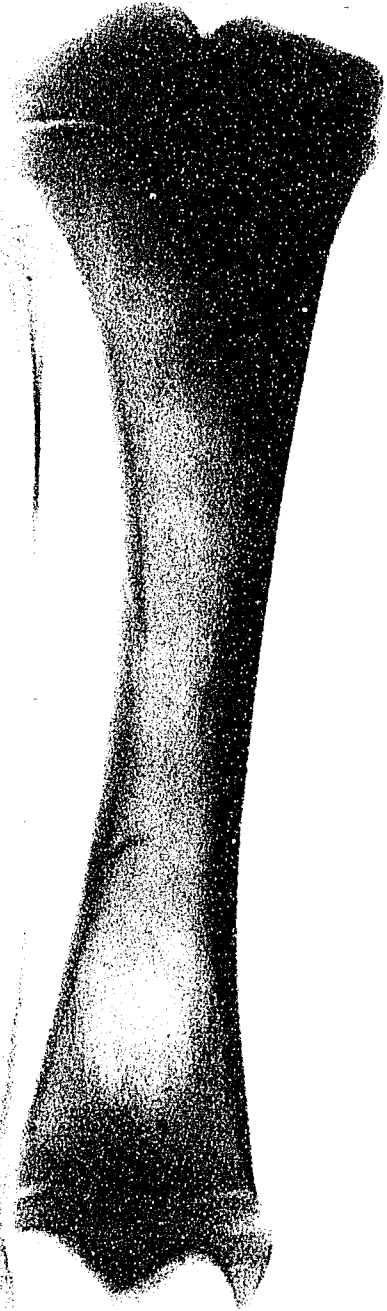


Figure XXII

Figure XXIII

Ovary of hypophysectomized animal S2, left; control, right.

Figure XXIV

Section of ovary of hypophysectomized pregnant sow S1. Hematoxylin-eosin. 30X.

1. Connective tissue.
2. Follicle.

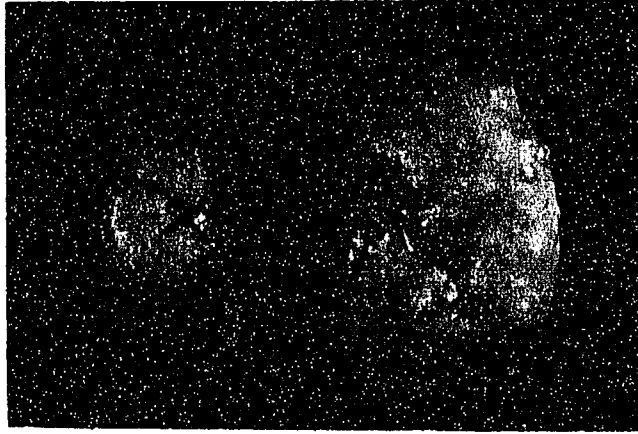


Figure XXIII



Figure XXIV



Figure XXV

Section of ovary of hypophysectomized animal S2. Hematoxylin-eosin. 30X.

1. Medullary area.
2. Small follicles of cortical area.

Figure XXVI

Section of ovary of control. Hematoxylin-eosin. 30X.

1. Follicle with ovum.
2. Corpus albicans.
3. Cell nests.



Figure XXV



Figure XXVI

Figure XXVII

Section of uterus of hypophysectomized animal S2. Hematoxylin-eosin. 200X.

1. Epithelium.
2. Gland.

Figure XXVIII

Section of uterus of control. Hematoxylin-eosin. 200X.

1. Epithelium.
2. Gland.

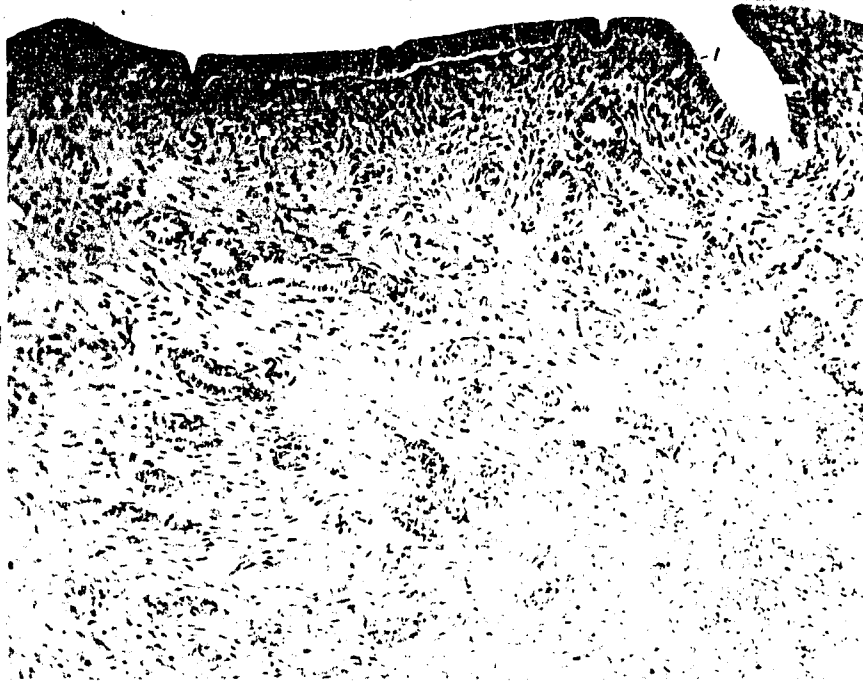


Figure XXVII



Figure XXVIII

Figure XXIX

Section of vagina of hypophysectomized animal S2. Hematoxylin-eosin. 200X.

1. Epithelium.

Figure XXX

Section of vagina of control. Hematoxylin-eosin. 200X.

1. Epithelium.

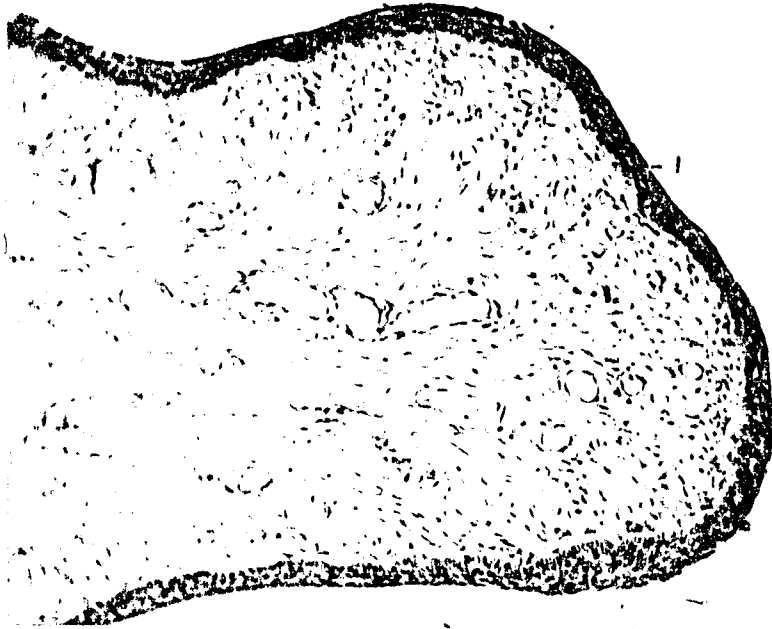


Figure XXIX



Figure XXX

Figure XXXI

Section of testis of hypophysectomized animal B3. Hematoxylin-eosin. 800X.

1. Interstitial cells.
2. Seminiferous tubules.

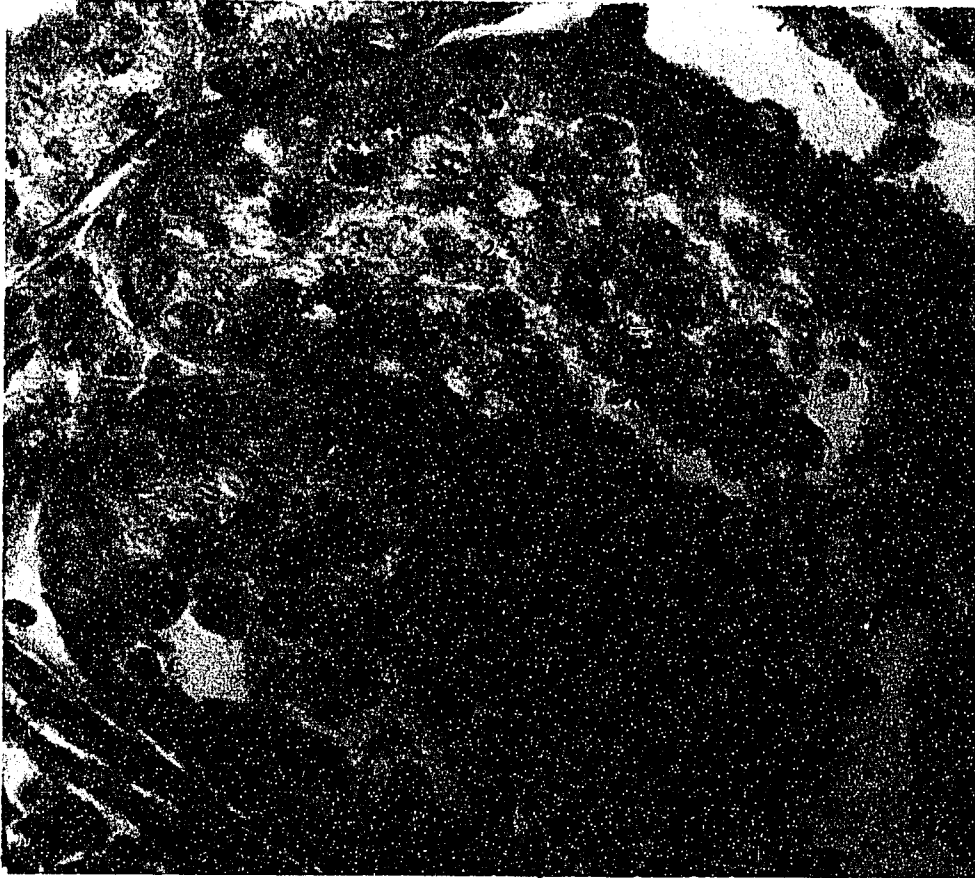


Figure XXXI



Figure XXXII

Section of testis of control. Hematoxylin-eosin. 800X.

1. Interstitial cells.
2. Seminiferous tubule.

Figure XXXIII

Section of testis of partially hypophysectomized sexually immature pig B7. Hematoxylin-eosin.

1. Interstitial cells.
2. Seminiferous tubule.

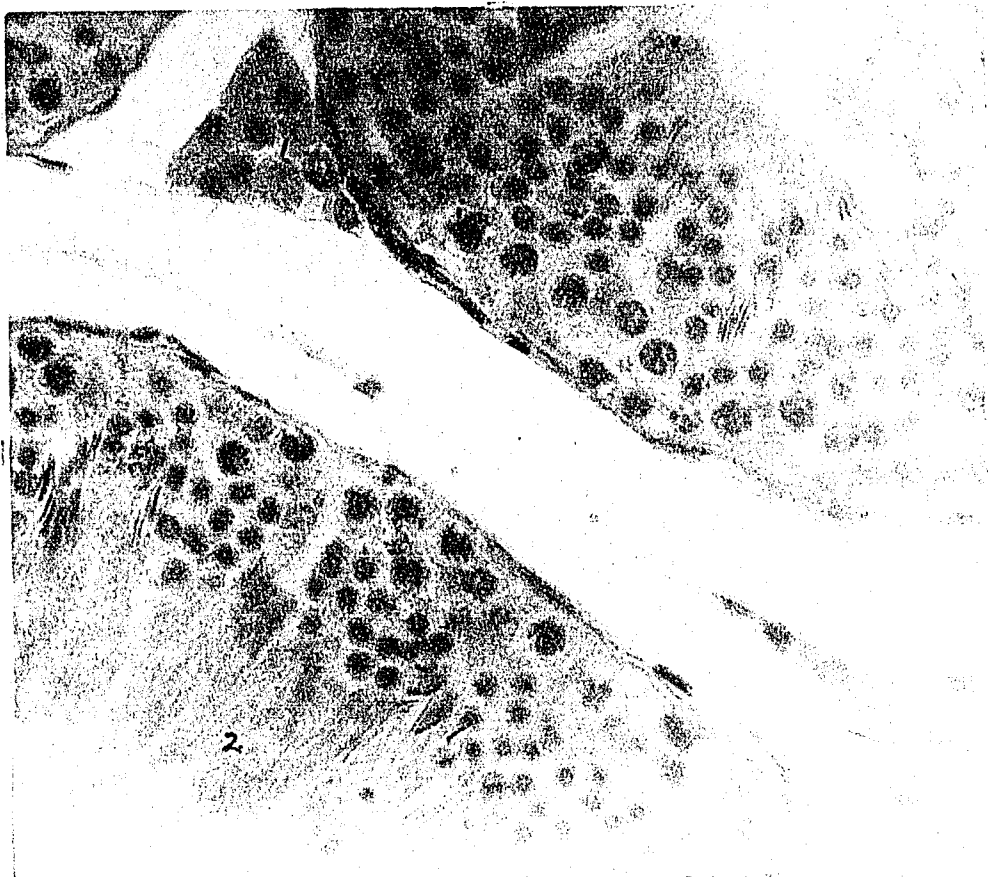


Figure XXXII



Figure XXXIII

Figure XXXIV

Section of prostate gland of hypophysectomized animal B3. Hematoxylin-eosin. 200X.

1. Acinus.
2. Septum.

Figure XXXV

Section of prostate gland of control. Hematoxylin-eosin. 200X.

1. Acinus.
2. Septum.

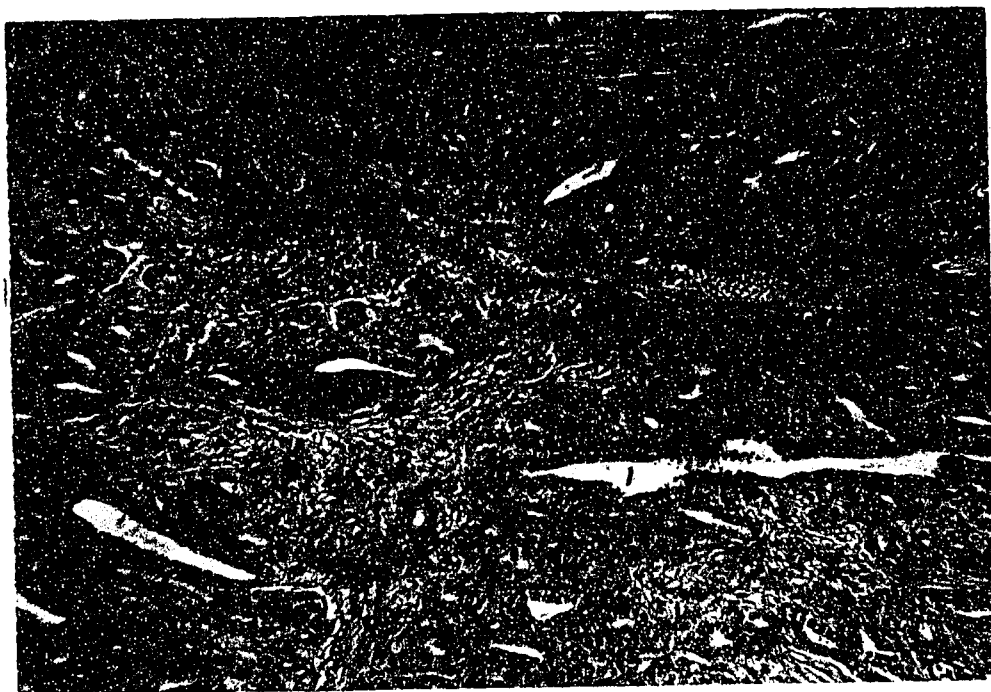


Figure XXXIV

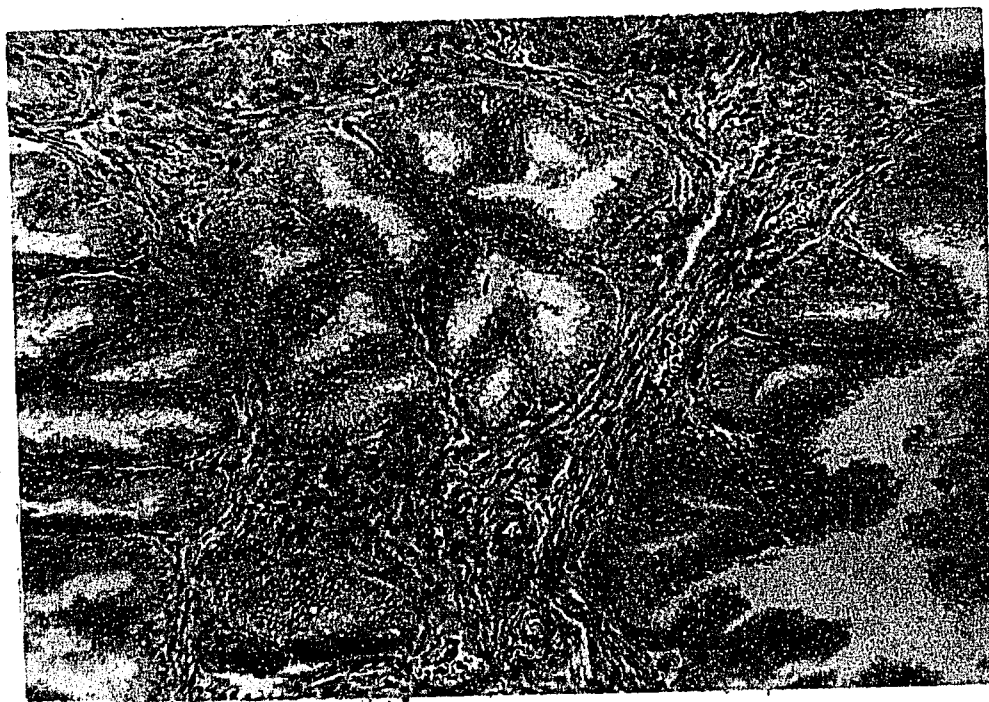


Figure XXXV

Figure XXXVI

Section of seminal vesicle of hypophysectomized animal B3. Hematoxylin-eosin. 200X.

1. Acinus.
2. Septum.

Figure XXXVII

Section of seminal vesicle of control animal. Hematoxylin-eosin. 200X.

1. Acinus.
2. Septum.

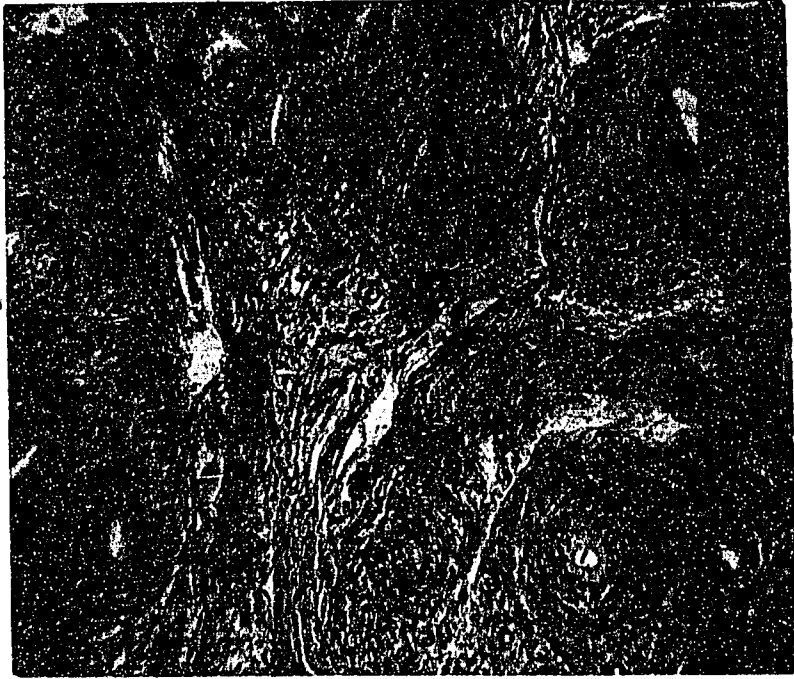


Figure XXXVI

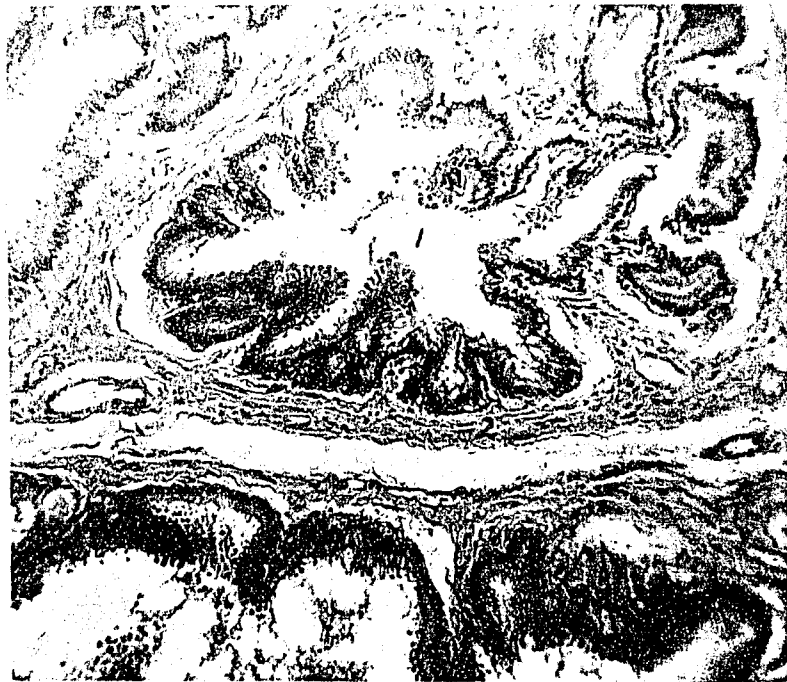


Figure XXXVII

Figure XXXVIII

Section of bulbo-urethral gland of hypophysectomized animal B3.  
Hematoxylin-eosin. 200X.

1. Acinus.
2. Septum.

Figure XXXIX

Section of bulbo-urethral gland of control. Hematoxylin-eosin.  
200X.

1. Acinus.
2. Septum.

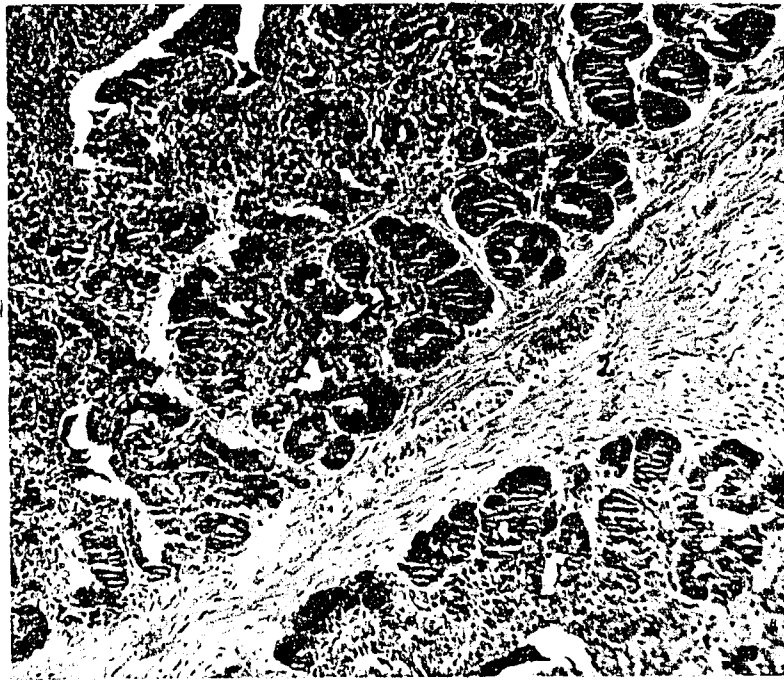


Figure XXXVIII

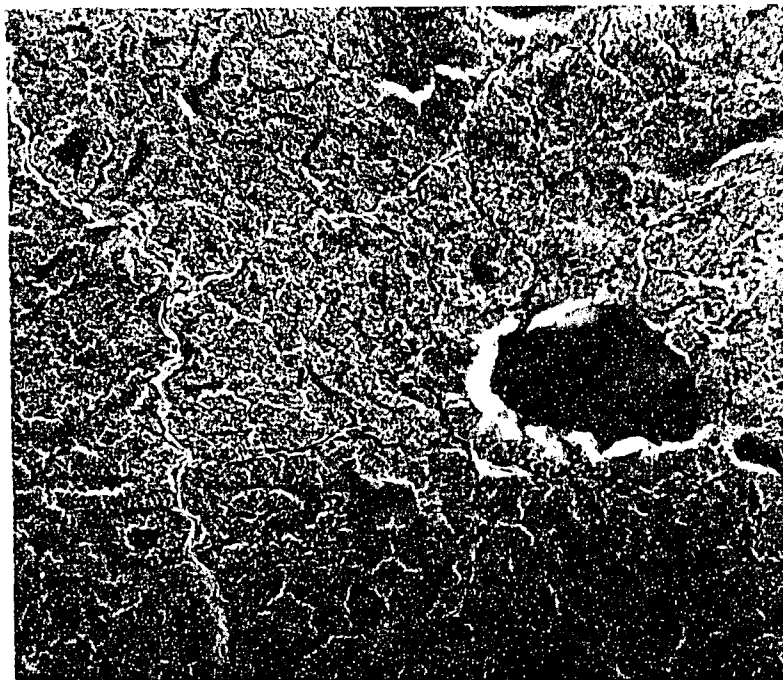


Figure XXXIX



Figure XL

Section of thyroid gland of hypophysectomized animal B2.  
Hematoxylin-eosin. 400X.

Figure XLI

Section of thyroid gland of hypophysectomized animal S2.  
Hematoxylin-eosin. 400X.



Figure XL

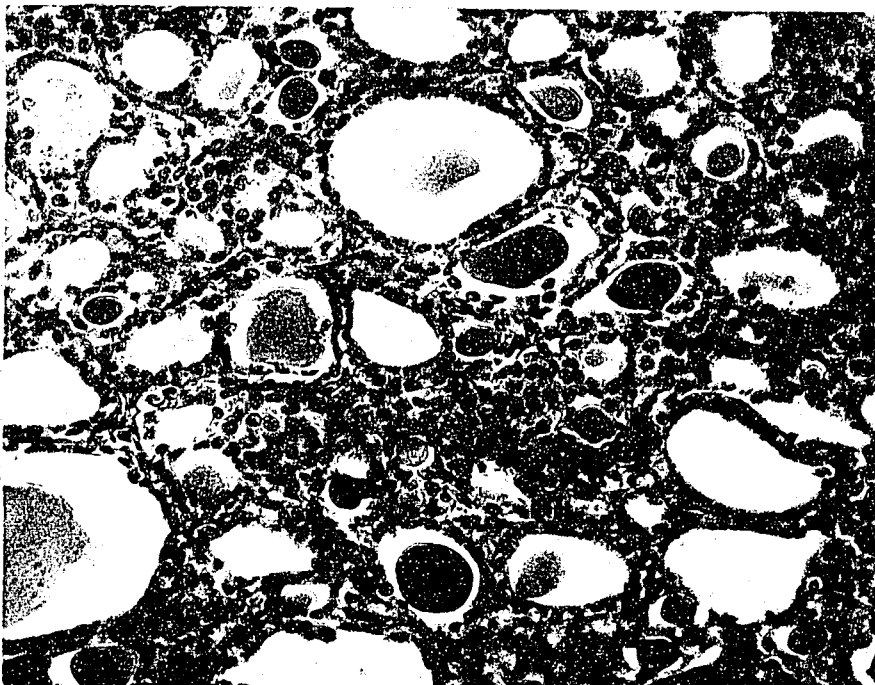


Figure XLI

Figure XLII

Section of thyroid gland of control. Hematoxylin-eosin. 400X.

Figure XLIII

Section of adrenal gland of hypophysectomized animal B3.  
Hematoxylin-eosin. 100X.

1. Glomerular zone.
2. Fascicular zone.
3. Reticular zone.
4. Medulla.

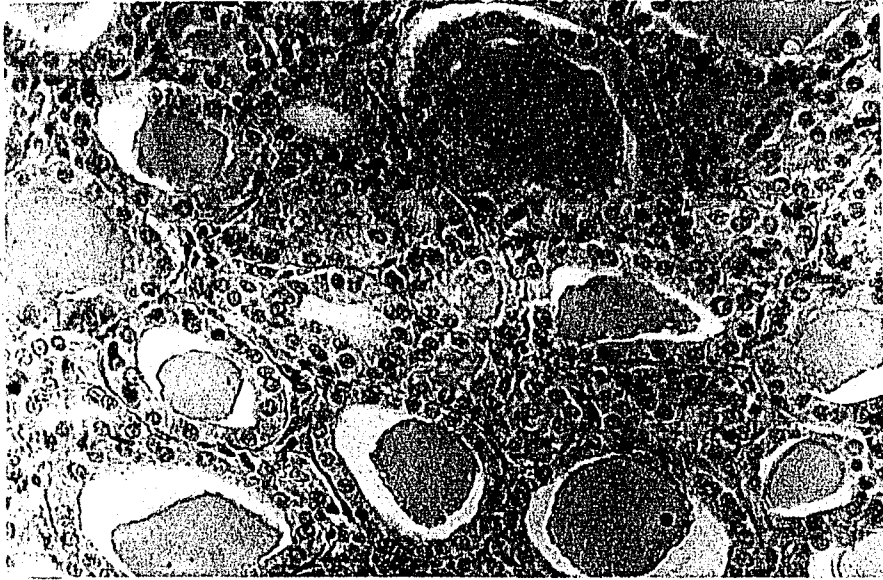


Figure XLII



Figure XLIII

Figure XLIV

Section of adrenal gland of control. Hematoxylin-eosin. 100X.

1. Glomerular zone.
2. Fascicular zone.
3. Reticular zone.
4. Medulla.

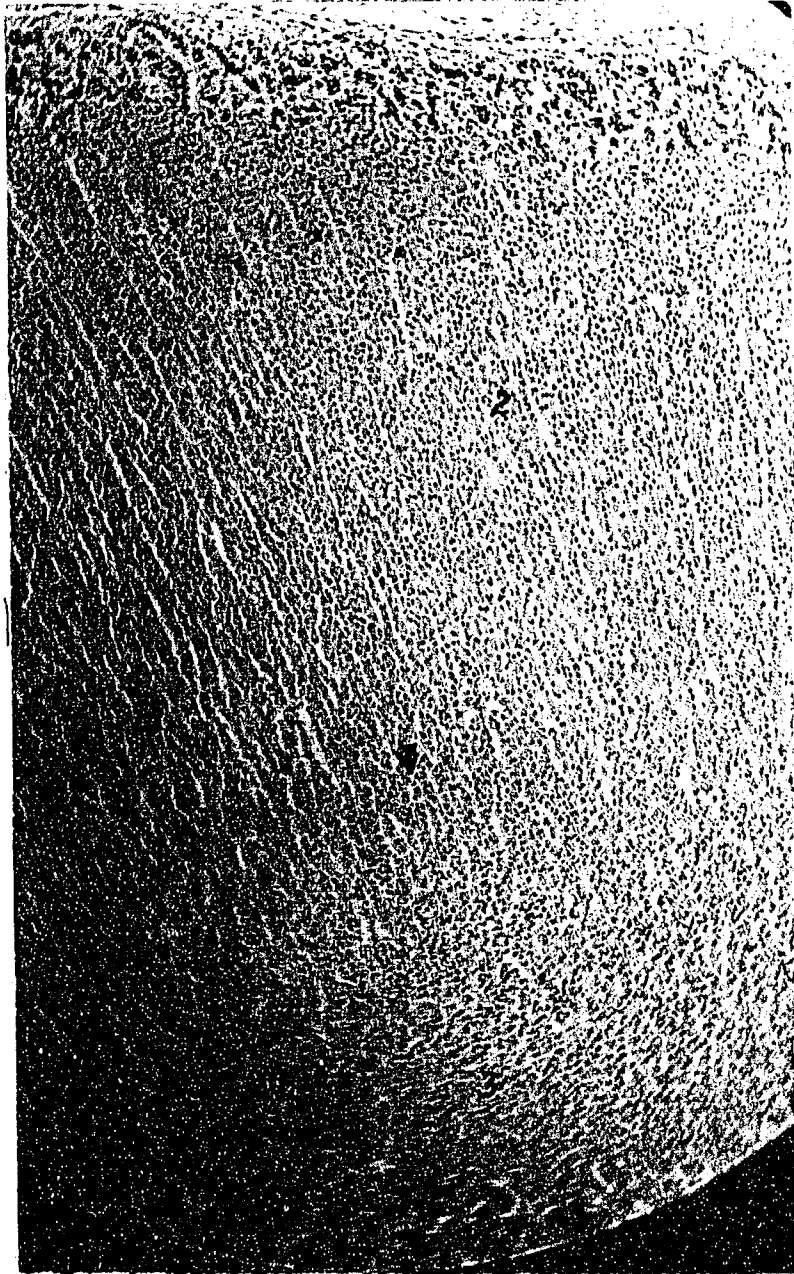


Figure XLIV

A P P E N D I X

Table 2  
Cell count of the anterior lobe

Animal	Alpha (%)	Beta (%)	Chrom. (%)	Sections	Fields	Cells
Sex. immature	38.9	9.1	52.0	3	30	6795
	41.7	16.1	42.2	3	30	6274
	42.3	11.2	46.5	3	30	4675
	37.4	12.0	53.7	3	30	4549
	32.6	12.0	55.4	3	30	5623
average	38.6	11.5	49.9	total 15	150	27916
Sex. mature female diestrus	55.8	8.7	35.5	3	30	4589
	55.1	7.7	37.2	3	30	3446
	48.3	15.6	36.1	3	30	4215
average	53.1	10.6	36.3	total 9	90	12250
Sex. mature male	58.3	11.8	29.9	3	30	3668
	56.5	9.7	33.8	3	30	3692
average	57.4	10.7	31.9	total 6	60	7360
Sex. mature average	55.25	10.65	43.1	total 15	150	19610



Table 3  
Organ and gland weights in grams

Animal <sup>a</sup>	Weights <sup>b</sup> (pounds)	Days <sup>c</sup> Lived	Gland <sup>d</sup> State	Liver	Heart	Spleen	Left Kidney	Right Kidney	Thymus	Pancreas
BC1	50-88	73	control	940	158	56	61	57	27.2	56
BN1	125		normal							54
BN2	90		normal							40.2
B1	46-47	17	complete	562	109	53	37	32	18	29.5
B2	45-76	82	complete	653	114	45	49	48	21	41
B3	38-79	89	complete	690	118	41	31.5	48	15.4	54.5
B4	55-107	69	partial	1143	198	52	91	95	79	60
B5	30-80	102	partial	817	148	48	70	67	24.7	53
B6	55-72	73	partial	559	117	41	72.5	73	26.4	38
B7	37-79	69	partial	656	118	62	50.5	52.9	14.3	31.1
SC1	55-100	88	control	911	170	56	78	71	29	49
SN1	83		normal							60
S1	208	174	complete							77.6
S2	66-99	86	complete	1014	167	54	94	89	26.4	61
S3	38-88	71	partial	938	139	59	62	60	14.8	38
S4	37-66	81	partial	811	128	56	69	66	35.5	40

<sup>a</sup> BC - control male, BN - normal male (not used as experimental control), B-hypophysectomized

<sup>b</sup> First weight, when experiment started, second, at time of necropsy.

<sup>c</sup> Days from beginning of experiment to necropsy.

<sup>d</sup> The amount of pituitary gland removed by the operation.



	Thymus	Pancreas	Thyroid	Left Adrenal	Right Adrenal	Left Ovary	Right Ovary	Left Testis	Right Testis	Left Sem.Vesc.	Se
	27.2	56	2.89	2.3	2.1			79.1	70.3	24.6	
		54	6.8	2.85	2.78			118	110	19.5	
		40.2	3.8	3.1	2.95			140	137	13.7	
	18	29.5	1.26	.6	.55			13	11.5	1.68	
	21	41	2.7	1.05	.95						
	15.4	54.5	2.81	.78	.71			33	33.5	.62	
	79	60	5.1	2.4	2.2			100	87	9.3	
	24.7	53	3.85	1.2	.87			102	111	18.7	
	26.4	38	1.67	.73	.6			62.5	58	3.07	
9	14.3	31.1	1.15	.75	.68			94	113	12.7	
	29	49	2.38	2.02	2.04	2.95	2.34				
		60	2.66	1.14	1.05	2.16	2.08				
		77.6	6.03	2.37	1.93	1.99	1.62				
	26.4	61	2.53	1.74	1.55	.425	.405				
	14.8	38	1.55	.94	.86	2.23	1.29				
	35.5	40	2.87	1.35	1.27	2.22	2.15				

B-hypophysectomized male, SC-control female, SN-normal female, S-hypophysectomized female.



ght vary	Left Testis	Right Testis	Left Sem.Vesc.	Right Sem.Vesc.	Prostate	Left Bulbo.- Ureth.	Right Bulbo.- Ureth.	Pituitary
	79.1	70.3	24.6	25.4	1.16	13.6	12.7	.185
	118	110	19.5	19.1	1.94	24.5	25.5	.215
	140	137	13.7	14.7	1.48	22.2	20.7	.195
	13	11.5	1.68	1.49	.34	3.37	2.57	
	33	33.5	.62	.59	.35	1.7	1.6	
	100	87	9.3	9.9	1.39	24	23	
	102	111	18.7	20.4	1.57	17.6	17.6	
	62.5	58	3.07	2.9	.72	6.1	4.9	
	94	113	12.7	11.7	1.52	11.6	11.5	
2.34								.175
2.08								.155
1.62								
.405								
1.29								
2.15								

, S-hypophysectomized female.

