UROLOGICAL PATHOLOGY

HERBUT

VOLUME II

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BY

Peter A. Herbut, M.D.

Professor of Pathology, Jefferson Medical College and Director of Clinical Laboratories, Jefferson Medical College Hospital, Philadelphia, Pennsylvania

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PREFACE

THIS work on Urological Pathology is intended for the general practitioner, the medical student, the general surgeon, the gynecologist, and the urologist. In short, it is intended for anyone interested in diseases of the urinary system or the male genital tract. Its aim has been to assemble and make readily available pertinent surgical pathologic data within the bounds of two volumes.

The contents are confined to disorders generally included in the specialty of Urology. In order to orient the reader some of the more important basic facts pertaining to embryology, anatomy, and physiology are briefiy summarized before the disease processes are discussed. In writing the work your author had the choice of presenting the material from a disease point of view, that is, carry the description of one disease process throughout the various portions of the genito-urinary tract, or of presenting the material from a regional point of view, that is, discuss the different diseases as more or less separate entities in each of the components of the genito-urinary system. Although the latter approach is inevitably accompanied by a certain degree of overlapping, it was chosen as being more practical because the surgeon, in operating, for example, on the prostate, or the pathologist, in examining the surgically removed specimen, wants to know above all what that particular prostatic lesion is and, at the moment, does not especially care about the appearance of a similar process in the kidney or the testis. Accordingly, the different diseases of each portion of first the urinary and then the male genital tract have been described in a systematic manner under the headings of congenital anomalies, inflammations, tumors, and mechanical disturbances. Further, in order to make desirable data readily available to the reader, each disease has been discussed under definition, distribution, cause, gross appearance, microscopic appearance, spread (in connection with tumors), complications, clinico-pathologic correlation, diagnosis, treatment, and prognosis. Throughout the work, except in the case of certain rare diseases, this outline has been rigidly adhered to. While much of the clinical data presented is admittedly more or less outside of the realm of surgical pathology, it has been included not only to bring to life what might otherwise appear to be a rather dead subject but also to broaden the usefulness of the volumes.

In order to accomplish the aims set forth, the literature of the last twenty to twenty-five years has been reviewed and the following textbooks have at one time or another been freely consulted.

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Despite the appearance of a work under a single authorship its writing must always be a cooperative venture, for without the loyal support of a host of enthusiastic colleagues the task would be unsurmountable. Among others, your author wishes to express sincere appreciation to the following for a job well done: Dr. Joseph F. McCloskey for the arduous task of proofreading, Dr. Philip T. Chu for the original line drawings, Mr. Allen F. Hancock for the photography, Mr. Robert T. Lentz and staff for library assistance, and Misses Gladys G. Urban, Jeanne C. McNaul, and Lucille S. Holmes for the secretarial work. Finally, your author wishes to thank Lea & Febiger for their encouragement, support, and wholehearted cooperation.

PETER A. HERBUT

Philadelphia, Pa.

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ADRENALS

EMBRYOLOGY

THE body contains two adrenal glands each of which consists of two entirely separate portions—the cortex and the medulla.

The *cortex* develops in two parts—the provisional and the permanent. The *provisional cortex* is identifiable in the 8 mm. embryo as a dorsal proliferation of peritoneal epithelium at the level of the root of the mesentery. The accumulating cells, one group on each side of the body, soon produce a large easily detectable condensation which projects from the dorsal wall of the celom between the urogenital organs and the mesentery. The provisional cortex is also known as the X or androgenic zone and constitutes most of the organs at the time of birth. Postnatally the original substance declines but involution is not complete until the age of two years. The *permanent cortex* appears almost as soon as the primitive cortex is formed. It consists of cells arising from the original focus of peritoneal epithelium. The proliferating cells first envelop and then penetrate the central portion of the original adrenal substance. Differentiation occurs gradually so that at birth the glomerular zone is seen next to the capsule and within the next few months the remaining zones appear.

The *medulla* is formed of chromaffin cells derived from the primitive ganglia of the celiac plexus. Invasion of the medial side of the provisional cortex is seen by the seventh week of embryonic life and continues until the end of fetal life. At this time the cells are permanently grouped in cords and masses in the central portion of the adrenal.

Although the adrenals generally develop from two separate foci, one on each side of the body, occasionally *multiple primordia* are seen or secondarily separated portions of the parent gland appear thus giving rise to accessory adrenal glands. Such accessory structures consist usually of cortical tissue only. Generally they are found within the kidneys, but they may migrate from their original position along the course of descent of the genital glands. The topic is discussed further in the section on congenital anomalies, p. 700.

ANATOMY

Gross Appearance.—The adrenal gland is also known as the adrenal body, adrenal capsule, suprarenal body, suprarenal capsule, and suprarenal gland. Normally the body contains two adrenal glands, one on each side of the vertebral column located immediately above and anterior to the upper pole of the corresponding kidney. The right gland is triangular in shape and is often referred to as resembling a cocked hat (Figs. 299 and

300). The left gland is crescentic in outline. It is somewhat larger and is situated at a slightly higher level than the right gland. Although the size is variable, the usual dimensions are length 3 to 5 cm., width 2 to 4 cm., and thickness 0.4 to 0.6 cm. The average weight is between 3.5 and 5 grams. From without in, each adrenal consists of fatty areolar tissue, capsule, cortex, and medulla.

Relations.—The *right adrenal* is located behind the inferior vena cava and right lobe of the liver and in front of the diaphragm and upper end of the right kidney. It has two surfaces. The *anterior surface* is directed

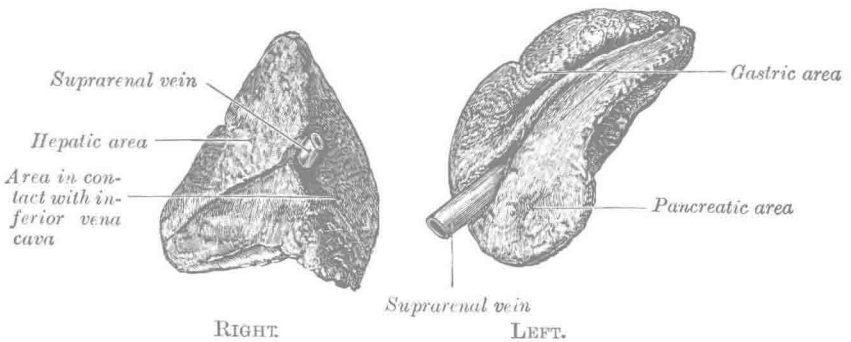

FIG. 299.—Adrenal glands—anterior view. (Gray's Anatomy.)

FIG. 300.—Adrenal glands—posterior view. (Gray's Anatomy.)

anteriorly and laterally. Its narrow nonperitoneal medial portion lies behind the inferior vena cava, while its upper nonperitoneal and lower peritoneal lateral portions are covered by the liver. A hilum containing the adrenal vein is located a little below the apex near the anterior border. The *posterior surface* contains a curved ridge which divides the gland into an upper portion that rests upon the diaphragm and a lower portion that rests upon the upper and anterior surface of the kidney.

The *left adrenal gland* is crescentic in shape and slightly larger than the right. It discloses a convex medial border, a concave lateral border, a narrow upper end, and a rounded lower end. The upper end of the *anterior*

surface is covered by peritoneum of the omental bursa which separates the gland from the stomach, while the lower end is free of a peritoneal covering and is related directly to the pancreas and the lienal artery. The hilum is located in the lower end of the anterior surface. The *posterior surface* is traversed by a vertical ridge which separates the gland into a lateral portion that rests against the kidney and a medial portion that rests against the left crus of the diaphragm.

Arteries.—Each adrenal gland receives its arterial supply from a surrounding plexus. The plexus is fed principally by three arteries—(1) superior suprarenal artery which arises from the inferior phrenic artery and this in turn arises from the aorta, renal artery, or the celiac artery, (2) middle suprarenal artery which arises from the aorta opposite the superior mesenteric artery, and (3) inferior suprarenal artery which arises from renal artery. The adrenal plexus in turn gives rise to three sets of arteries—one set to the capsule, another set to the cortex, and a third set to the medulla.

Veins.—Each adrenal gland contains one vein which emerges from the hilum. The right ends in the inferior vena cava, while the left terminates in the left renal or the left inferior phrenic vein.

Lymphatic Vessels.—The lymphatic vessels usually accompany the suprarenal vein and end in the lateral aortic lymph nodes. Occasionally some of the vessels pierce the corresponding crus of the diaphragm and end in the lymph nodes of the posterior mediastinum.

Nerves.—Each adrenal gland is well supplied with nerves. They arise from the celiac and renal plexuses, the celiac ganglion, the phrenic nerves, and the greater splanchnic nerves. The nerves enter the lower and medial part of the capsule, traverse the cortex, and end in numerous small ganglia in the medullary portion of the gland.

Microscopic Appearance.—The histologic components of each adrenal gland to be considered are: periadrenal tissue and capsule, cortex, and medulla.

The *periadrenal tissue* is composed essentially of connective tissue and fat cells. The *capsule* of the adrenal consists of rather dense connective tissue that sends prolongation into the adjacent cortex and that contains arteries, nerve plexuses, and sympathetic ganglion cells.

The *cortex* is the external portion of the adrenal gland proper. Normally it consists of the following three layers: outer zona glomerulosa, middle zona fasciculata, and inner zona reticularis (Fig. 301). The *zona glomerulosa* is located immediately within the capsule. It is composed of ovoid groups or arc-like collections of closely packed, small columnar cells, the free edges of which join capillaries. The cell borders are fairly sharply demarcated. The cytoplasm is scanty and contains irregular clumps of basophilic material and a few tiny droplets of lipoid material. The latter are generally located between the nucleus and the border of the cell which faces the capillaries. The nuclei are rounded, sharply defined, and deeply stained. The cells of the zona glomerulosa merge gradually with the cells of the *zona fasciculata*. This is the widest zone and constitutes the bulk of the cortex. Its cells are polyhedral and somewhat larger than are those of the zona glomerulosa. The cell borders are distinct. The cytoplasm is lace-

like and contains numerous lipoid droplets. The nuclei are single or double, centrally located, vesicular, and near the inner portion frequently disclose mitoses. The innermost zone of the cortex—the *zona reticularis*—is composed of cords of cells forming an anastomotic network. The outer cells of this zone are similar to the cells of the zona fasciculata, although they contain a smaller amount of lipoid material. The inner cells are of two types—dark and light. The *dark cells* are rather small, disclosing deep homogeneously eosinophilic staining cytoplasm and small, round, extremely basophilic nuclei. They are rich in both lipoid material and clumps of yellow or brown pigment. The *light cells* are larger and have rounded contours. They contain granular, pink staining cytoplasm and rather large, pale staining, vesicular nuclei. Unlike the dark cells they reveal little lipoid material or brown pigment.

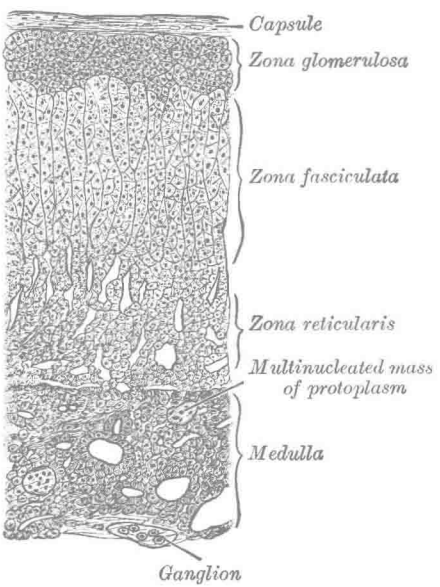

FIG. 301.—Histologic appearance of the adrenal gland. (Gray's Anatomy.)

The *medulla* occupies the central portion of the adrenal gland. Its demarcations from the cortex are irregular despite the fact that they are quite distinct. The cells of the medulla form part of the *chromaffin system*. They are irregularly distributed and are arranged in rounded groups or short cords surrounded by sinusoids. They are generally polyhedral in outline, sharply defined, and possess an abundant amount of granular, lightly eosinophilic cytoplasm, and round, evenly but deeply staining nuclei. When fixed in a fluid containing postassium dichromate or in chromic acid fine brown granules are discernible in the cytoplasm. This reaction is spoken of as the chromaffin reaction and is said to be due to the oxidation and polymerization of epinephrine (adrenaline). Aside from the chromaffin cells, the medulla contains also *ganglion cells* and collections of small round cells. The former are single or grouped and are composed of large

polyhedral, sharply defined cells with somewhat basophilic cytoplasm containing occasional coarse brown granules. The nuclei are large, rounded, and deeply staining. The ganglion cells produce axons which end around the chromaffin cells. The collections of *small round cells* vary in number from few to many. They have the appearance of and probably represent lymphocytes, although they may also be the progenators of sympathoblasts (neuroblasts) and medullary cells.

PHYSIOLOGY

Since the adrenal gland is a composite organ, the secretions produced by each of the two components—medulla and cortex—vary greatly and should therefore be considered separately.

Medulla.—The functions of the medulla are controlled entirely by nerves. Its main secretion is a secondary alcohol called adrenaline (known also as adrenalin, epinephrine, adrenin, and suprarenin). The following are the generally accepted probable steps in its production. Tyrosine is oxidized possibly by way of tyrosinase to dihydroxyphenylalanine ("dopa"). This substance then by enzymatic decarboxylation is transformed into dihydroxyphenylethylamine which upon the addition of a hydroxyl group is transformed into noradrenaline. The addition of a methyl group to noradrenaline results in the formation of adrenaline.

Noradrenaline comprises about 18% of adrenaline extracted from the adrenal medulla. This substance is entirely a vasoconstrictor, has little effect upon the cardiac output, has more effect upon the uterus of a pregnant cat than does adrenaline, but is less powerful than adrenaline in its other actions.

Adrenaline imitates the effects evoked by stimulation of the sympathetic system and is therefore called a sympathomimetic drug. Its point of action is said to be a hypothetical substance surrounding the termination of the nerve fibers. Briefly and in general the actions of adrenaline may be listed as follows: stimulation of uterine muscle, raising of blood pressure by way of vasoconstriction, inhibition of the muscles of the bowel, dilatation of the coronary arteries, intimate connection with carbohydrate metabolism, and stimulation of ACTH (adrenocorticotropic hormone) secretion. The centers of control of the physiologic functions of the adrenal medulla are located in the upper part of the floor of the fourth ventricle and in the hypothalamus. The adrenal medulla is not essential to life, for upon its disappearance other organs of the chromaffin system take over its functions.

Cortex.—Unlike the medulla the adrenal cortex is essential to life, for removal of more than five-sixths of its bulk results in death. In dogs the average survival time after complete adrenalectomy is in the neighborhood of ten days. Pregnant animals or those in heat, however, survive several days longer due probably to the increased amount of progesterone. The adrenal cortex is the source of many *hormones* the production of which appears to be governed entirely by the adrenocorticotropic hormone (ACTH) of the pituitary gland. Some of the known steroids produced by the adrenal cortex can be grouped physiologically into the following four major categories: (1) *S* or *sugar* hormones consisting of *corticosterone*,

dehydrocorticosterone, and *cortisone* (*compound E*). Some of the actions of this group of hormones as a whole are (*a*) gluconeogenesis (from proteins) resulting in hyperglycemia and increase in glycogen stores, (*b*) postponement of muscular fatigue, and (*c*) supposedly responsible for the manifestation of the stress reaction. In addition cortisone has been found to have a salutary effect on arthritis (ACTH acts similarly by simulating the output of adrenal steroids). (2) *Salt* and *water* hormone consisting of *desoxycorticosterone.* Its functions are (*a*) to increase the plasma volume, (*b*) to increase the sodium in body fluids and cells, and (*c*) to reduce the potassium in body fluids and cells. (3) *N retaining* hormone consisting of *androgenic* factors. Overproduction of androgenic factors results in (*a*) masculinization in the female, (*b*) pseudohermaphroditism, and (*c*) sexual precosity in prepuberal males. (4) *Estrogenic* substances. The presence of these substances is evidenced by the fact that they can be extracted from the adrenal cortex and that rare adrenal tumors cause feminization in the male. The corresponding measurable *urinary excretion products* of these cortical hormones are as follows: (1) S or sugar hormones appearing as "corticoids," (2) salt and water hormone appearing as pregnandiol (?), (3) N retaining hormone (androgenic factors) appearing as 17-ketosteroids, and (4) estrogenic substances appearing unchanged.

The *response* of an animal *to* any *stress* requires the presence both of the cortex and the medulla or its equivalent. The generally accepted theory is that the immediate reaction is the production of adrenaline. This stimulates the formation of the adrenocorticotropic hormone of the anterior pituitary which acts upon and liberates hormones from the adrenal cortex. The cortical hormones in turn bring about a disintegration of lymphocytes with resulting lymphopenia, atrophy of the lymphoid tissue, and increase of the beta and gamma globulin of the serum. This set of events forms a portion of the "alarm reaction of Selye." That the response is mediated by adrenocortical hormones is indicated by the fact that it cannot be brought about if the adrenal cortex is removed (Maximow and Bloom).

PATHOLOGY

CONGENITAL ANOMALIES

General Considerations

The varieties of developmental malformations of the adrenal gland are relatively few and most of those which do occur are of little or no significance from a surgical point of view. The following abnormalities may be briefly considered in the order mentioned: absence, hypoplasia, atrophy, aberrant adrenal tissue and heterotopia, and myeloid formation.

Absence

Complete absence of both adrenal glands is extremely rare and is, of course, incompatible with life. Absence of one adrenal gland is not too uncommon and is entirely consistent with a normal existence provided the

opposite gland is present and is undiseased. The condition looms forth as an important consideration when the contralateral organ is affected by a tumor which necessitates its removal. When one adrenal gland is absent the other usually undergoes compensatory hypertrophy.

Hypoplasia

Hypoplasia of the adrenal gland connotes underdevelopment. It is generally agreed that the cause of such an abnormality is a maldevelopment or hypoplasia of the pituitary gland (Hartman and Brownell). The condition is most commonly seen in anecephalia, microcephalia, hemicephalia, and congenital hydrocephalus. *Pathologically* the adrenal glands show varying degrees of reduction in size from almost normal to about one-sixth of the usual bulk. Generally it is the cortex that is mostly or solely involved, the medulla remaining comparatively well developed.

Atrophy

Atrophy of the adrenal glands is an acquired condition connoting a decrease in bulk once the glands have reached their normal proportions. About one-half of the cases of Addison's disease are accompanied by atrophy of the adrenal glands (Hartman and Brownell). The *cause* of bilateral atrophy is generally considered to be infection or toxic necrosis, the original manifestations of the disorder, however, being no longer

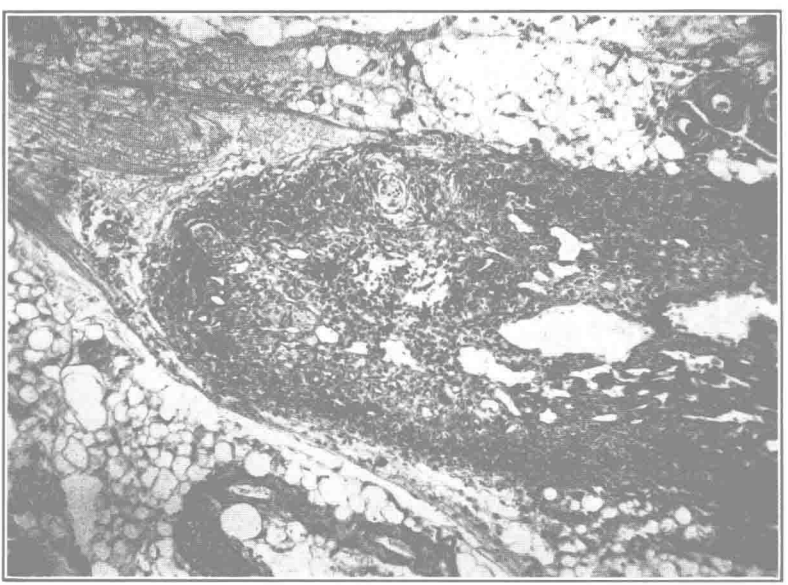

FIG. 302.—Atrophy of the adrenal from a case of Addison's disease. The cortical cells are entirely absent and the cortex is replaced with a band of fibrous tissue. The medullary cells while still present reveal considerable atrophy. × 100.

apparent. Theoretically ACTH insufficiency as a primary cause of atrophy in adults is possible but must be extremely rare. Unilateral atrophy of an adrenal gland may occur secondarily to hyperactivity of the remaining organ. *Pathologically* the gross appearance of the organs varies from almost normal to such that no adrenal tissue can be recognized grossly with certainty. Histologically, as in the case of hypoplasia, it is the cortices that are usually affected with medullas more or less intact (Fig. 302). Sometimes the cortical tissue undergoes irregular nodular regeneration.

Aberrant Adrenal Tissue

Definition.—Accessory, aberrant, or dystrophic adrenal cortical tissue connotes the presence of such tissue in abnormal locations. As already stated in the preceding chapter this should be distinguished from adrenal heterotopia which signifies a misplacement of the entire gland, there being no normal adrenal tissue present in the usual location on the affected side. While this differentiation is generally accepted by most observers the definition given by O'Crowley and Martland is somewhat confusing. They define complete adrenal heterotopia as the presence of the entire adrenal beneath the capsule of the kidney (in an abnormal location) and partial adrenal heterotopia as the presence of a large portion of the adrenal beneath the capsule of the kidney (or other abnormal locations). In either case they accept the absence of any adrenal tissue in the normal position. Since adrenal inclusions in the kidney have already been considered in Chapter V, they shall be omitted from discussion at this point.

Distribution.—While the presence of accessory adrenal cortical tissue in abnormal locations is quite common, the incidence of true adrenal heterotopia is in comparison much less frequent. In 1939 Nelson reported on nineteen cases of accessory adrenal cortical tissue and reviewed the literature on the topic with regards to both humans and animals. He stated that accessory adrenal tissue in the vicinity of the adrenal gland was first described by Morgani in 1740 and at a distance from the adrenal gland by Marchand in 1883. The latter author described it as occurring in the free edge of the broad ligament near the ovary and between the lower pole of the kidney and the broad ligament. Nelson further stated that a concerted effort to find the incidence of accessory adrenal tissues in all locations has not been attempted, but that some figures are available regarding its frequency in specific sites. Thus accessory tissue under the capsule of the right lobe of the liver was found in four of 510 persons examined at autopsy within a period of seven months by one author and was found in twenty-three (76.5%) of thirty gonads examined by another author. In 1939 Culp reported on adrenal heterotopia with regards to its incidence in the kidney. He stated that the literature contained twenty-two cases in addition to the one recorded by him, and the male-female ratio was 2:1. In 1942 Gruenwald discussed in general the origin of tissues in regions where such tissues normally are not found paying special attention to adrenal cortical tissue. In 1943 O'Crowley and Martland wrote on adrenal heterotopia, rests, and so-called Grawitz tumor. They stated that true adrenal heterotopia was first described by Klebs in 1876. They reported on eight cases of bilateral

adrenal-renal heterotopia encountered in 5000 routine autopsies. Seven of these occurred in males and one in a female. In 1943 Peale and Smith reported on a unique case of adrenal cortical inclusion or Walthard's cell rest in a uterine fibroid. In 1944, Kepler, Dockerty, and Priestley summarized the literature on adrenal-like ovarian tumors associated with Cushing's syndrome. They stated that the previous literature contained thirteen examples of such a tumor. To these they added a personal case. In 1947 Östergaard reported on a case of feminizing tumor of the testicle which he designated as aberrant adrenocortical tumor in a male twenty-eight years of age. It was his opinion that the tumor arose from accessory adrenal cortical tissue in the hilus of the testis.

Cause.—The cause of adrenal *heterotopia* (usually beneath the capsule of the kidney but sometimes beneath the capsule of the liver) is probably a more intimate association of the adrenal gland with these organs than is normally found. The theories regarding the causes of *accessory adrenal cortical tissues* in abnormal locations may be briefly listed under three headings (Culp and Gruenwald): (1) Fragments of cortical tissue may split off as the medullary elements migrate into cortical anlage. Most of these remain near the parent gland, but some become included in or are dragged along with such structures as the sex organs. (2) The approximation of the adrenal tissue to developing adjacent organs may be more intimate than that normally present and portions of the adrenal cortex may thus be incorporated within the structures, and (3) Activation of latent potencies which are normally present but not activated in the region bearing the abnormal tissue. This theory holds that large areas of the posterior abdominal wall have the ability to form cortico-adrenal cells as, for example. the kidney has the potency to form cortico-adrenal tissue, the gonads have the capacity to form kidney cells since they develop from the tissue on the medial side of the mesonephros, *etc.*

Clinical Manifestations.—Ectopic adrenal tissue as such or true adrenal heterotopia is not accompanied by any clinical manifestations.

Gross Appearance.—The location of *aberrant* adrenal *cortical tissue* is generally at a point any place between the normal position of the adrenal gland and the path of descent of the testicle or ovary. In addition the liver is said to be a fairly frequent site of deposition and one case has been described in which the tissue was attached to the spinal portion of the eleventh cranial nerve. More specifically the *common locations* of accessory adrenal cortical tissue may be listed as follows: in the vicinity of the adrenal gland, beneath the renal capsule, along the spermatic or ovarian veins, at the inguinal ring, in the epididymis and testis, in a uterine fibroid (one case), in the free edge of the broad ligament, and within the ovary. In the epididymis and testis the disposition of tissue is as follows: mediastinum of the testis, tunics of the testis, connective tissue between the testis and epididymis, near the epididymis, and within the epididymis. According to Nelson there has not been a single case in which the tissue was found deep within the testis, and there is only one recorded case where the aberrant tissue was located underneath the tunica albuginea. *Grossly* the accessory tissue generally consists of a rounded or flat, sharply demarcated

deposit of orange-yellow or brown, rather soft tissue that usually measures 3 to 4 mm. and not more than 1.7 mm. in diameter.

Adrenal heterotopia is usually confined to the kidney or the right lobe of the liver. In each case the adrenal gland is located beneath the renal or hepatic capsule respectively. The condition was bilateral in seventeen of the twenty-two cases collected by Culp and it was bilateral in each of the eight cases recorded by O'Crowley and Martland. It is generally agreed that the misplaced gland is grossly similar to a normal gland except that the organ is, as a rule, smaller and may be thinner. It is also generally agreed that the heterotopic gland is composed not only of adrenal cortical tissue but also medullary substance both of which can be identified grossly

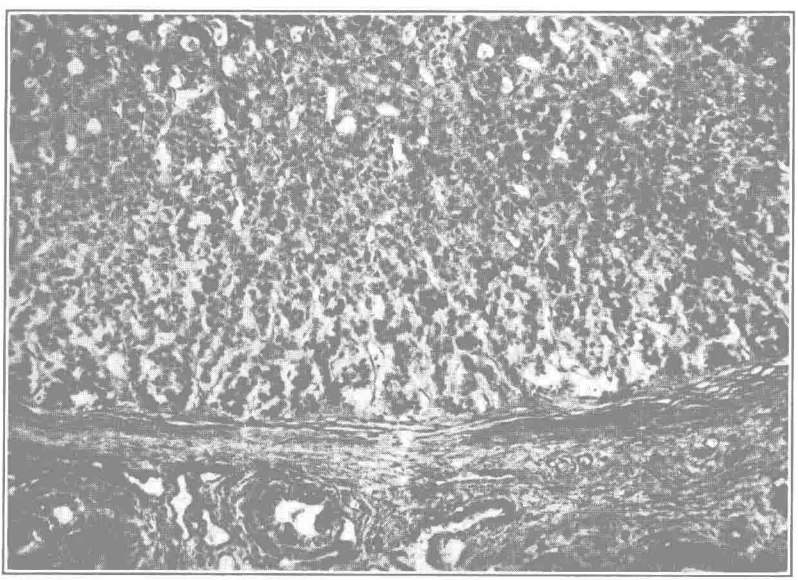

FIG. 303.—Ectopic adrenal cortical tissue in the vicinity of the epididymis. × 100.

(Culp). As already stated in the definition, however, O'Crowley and Martland maintain that only cortical substance is recognizable for it alone is present and that the medullary zone being absent is thus not apparent. As far as the kidney is concerned the abnormal gland is, as a rule, located in a saucer-like depression in its upper and anterior pole, that is, just inferior to the normal position of the adrenal gland. In each instance the misplaced gland is closely adapted to the renal substance disclosing an absence of the usual interposing connective or fibrous tissue. As already stated, the right adrenal may sometimes be found beneath the capsule of the right lobe of the liver. In all cases of true heterotopia there is no adrenal tissue in the usual location on the affected side.

Microscopic Appearance.—*Aberrant adrenal tissue* generally consists of adrenal cortex only (Fig. 303). The two outer zones, namely, zona glomeru-

losa and zona fasciculata, are as a rule present and easily identifiable, while the innermost zone, that is, the zona reticularis, may be present or absent. Histologically the cells forming the various portions of the cords are essentially the same as those in the normal adrenal gland. As already stated several times in this section, the histologic appearance of a *heterotopic adrenal gland* is not agreed upon due, of course, to the different concepts as to what constitutes such an organ. If the definition given at the beginning of this section is adhered to, the misplaced gland, except for being somewhat hypoplastic, discloses a definite cortex and medulla, and the cortex furthermore consists of the three well-recognized zones—outer zona glomerulosa, intermediate zona fasciculata, and inner zona reticularis. In your author's opinion the article by O'Crowley and Martland somewhat confused the issue in this respect, for as already stated they maintained that a heterotopic adrenal gland contains no medullary substance. Aside from this controversy it is generally accepted that a heterotopic adrenal gland is not separated from the renal or hepatic substance by a connective or fibrous tissue capsule, but on the other hand the parenchymal cells of each of the apposing organs are intimately associated with each other.

Complications.—Although generally ectopic adrenal cortical tissue or true adrenal heterotopia is not subjected to complications, Culp maintained that the latter is of definite *clinical significance*. In support of his contention he listed the following: (1) the kidney may be inadvertently removed at the time of operation under a mistaken diagnosis of malignant tumor, (2) after the removal of a heterotopic adrenal gland and corresponding kidney the patient may develop profound shock, (3) there is always a subsequent danger of operation on the remaining kidney if one adrenal had been previously removed, and (4) the chances of a patient developing adrenal insufficiency are greater following the inadvertent removal of a heterotopic adrenal gland. A serious *complication*, which is a possibility but which at present still lacks definite proof, is the development of a tumor from abnormal ectopic adrenal cortical tissue. The question of hypernephroma has already been considered in the previous chapter on the kidney, while a tumor arising in an adrenal rest of the testis has been described by Östergaard and at least fifteen similar tumors arising from adrenal rests have been described in the ovary.

Diagnosis.—A correct diagnosis cannot be made clinically. It is generally accomplished at the time of operation or at postmortem.

Treatment.—Surgical excision of accessory adrenal cortical tissue or of a heterotopic adrenal gland is contra-indicated unless a tumor is suspected.

Prognosis.—Except in the presence of a malignant tumor the prognosis is excellent.

Myeloid Formation

Definition.—By myeloid formation is meant the presence of bone marrow within the adrenal gland. The lesion has also been called bone marrow heterotopia, myeloid metaplasia, lipo-reticulo-endothelioma, benign bone marrow tumor, type of benign myeloma, lipoma, and myelolipoma. Since the lesion has been recorded only in adults it probably does not represent a congenital abnormality.