TUMORS OF THE ADRENAL

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ATLAS OF TUMOR PATHOLOGY

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TUMORS OF THE ADRENAL

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TUMORS OF THE ADRENAL

INTRODUCTION

True neoplasms of the adrenal glands are infrequent or rare. They include (1) those derived from cells peculiar to the adrenal, and (2) those derived from tissues in the adrenal not peculiar to that structure and common to other situations. The former are the lesions considered especially in this fascicle.

Of the latter, fibroma, myoma, neurofibroma, and lipoma are infrequent incidental findings. The so-called "osteoma" is probably a metaplasia following inflammation or hemorrhage. Both hemangioma and lymphangioma have been reported. Two "hemangioblastomas" have been reported (Marten and Meyer, Menon and Annamalai). So-called "cysts" of the adrenal are apparently either pseudocysts resulting from cystic degeneration of hematomas or adenomas, or are dilated angiomatous cavities (Reimann and Guyton). The latter are more frequent in the lymphangioma where the cavities are frequently multilocular.

The spindle and giant cell sarcomas of the older literature were probably anaplastic carcinomas. The "round cell" sarcomas would undoubtedly be classified today as sympathicogoniomas. In the last decade no verified cases of lymphosarcoma confined to the adrenal have been found. The fibrosarcoma described by Cran appears to be a true sarcoma, and myxosarcoma has been reported. Neoplasms should be distinguished from nodular lesions which resemble neoplasms.

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Menon, T. B., and Annamalai, D. R. A haemangioblastoma of the adrenal gland. J. Path. & Bact., 39:591–594, 1934.

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TUMOR-LIKE LESIONS

Hamartoma is the name given to a tumor-like malformation in which there is an abnormal arrangement and redundancy of cells and structures in themselves natural to the part or organ. A hamartoma may become a neoplasm. Lymphangioma and hemangioma are rare in the adrenal, but appear like similar lesions elsewhere. The cortical nodule is a tumor-like arrangement of cells like those of the adrenal cortex and is a hamartoma. The exact classification of the myelolipoma is not certain. If bone marrow is a natural component of adrenal, it is a hamartoma. However, if it is a tumor-like nodule arising from heterotopic inclusion of bone marrow, it is a choristoma. The pigmented nevus of the skin is usually classified as a progonoma because of resemblance to dermal organs of primitive species. However, if the nevus or the melanoma is primary in the adrenal, the term progonoma is not justified and the lesion is primarily a hamartoma and then a neoplasm.

Cortical Nodules. Synonyms and Related Terms: Noduli substantiae corticalis suprarenalis (Lat.); benign adenoma; cortical adenoma. When multiple and numerous, struma suprarenalis. When in other parts of the body, Marchand nodule, accessory adrenal, ectopic adrenal, or adrenal rest.

DEFINITION. Cortical nodules are spherical, well defined, usually encapsulated masses of cells like those of the adrenal cortex. They occur in the cortex, capsule, or apparently in the periadrenal fat.

ORIGIN. This is probably the result of pinching off of the cortex either during embryonal and fetal development, or during subsequent growth, particularly in the fourth and fifth decades when the adrenal may be an active participant in sexual involution.

CLINICAL FEATURES. None. Cortical nodules are an incidental observation in about one-third of the autopsies.

DESCRIPTION. The condition is usually bilateral. The nodules are usually spherical and vary in size within the same specimen. The diameter ranges from less than a millimeter to 3 or 4 centimeters. They are often multiple and usually small in number. The nodules are yellow and of about the same consistency as the adrenal. They are well-defined with a more or less distinct capsule. Infrequently, nonencapsulated forms occur. Serial sections of several specimens have demonstrated that those in the periadrenal fat are attached to the cortex by a pedicle of cortical cells or of connective tissues (figs. 1, 2, 3, 4, 5).

MICROSCOPIC. The capsule is of variable thickness in different nodules. It is composed of poorly vascularized, mature collagenous tissue. The cells of the nodule are arranged like those of the zona glomerulosa, sometimes with additional cords like the zona fasciculata, but only rarely like the zona reticularis. With great rarity, there is a semblance of acinus formation. The cells are about the same size as those of the adrenal cortex. The nucleus is vesicular. Multinucleated cells are rare. The cytoplasm is vesicular. The lipid content is about the same as in the neighboring cortex. The reticular zone cells may contain brown lipofuscin. When lipids are reduced in amount in the cortex, they usually remain in the nodules. Connective tissue stroma and capillaries are like those of the adrenal cortex.

DIFFERENTIAL DIAGNOSIS. There is no sharp line of distinction between a cortical nodule and a cortical adenoma. However, the cortical nodule is usually multiple and the adenoma single. The adenoma is usually larger than the nodule and often without the regularity of cellular arrangement of the nodule. It is suspected that a nodule may give rise to an adenoma, and, if that be true, may, through transformation of the nodule, be the ultimate source of a cortical carcinoma.

Reference

Nelson, A. A. Accessory adrenal cortical tissue. Arch. Path., 27:955–965, 1939.

Myelolipoma. Synonyms and Related Terms: Myelolipoma (Lat.); ectopic bone marrow; metaplastic bone marrow.

DEFINITION. This is a tumor-like mass of fatty tissue, usually beginning in the medulla but sometimes in the cortex, and composed of fat and cells like those of bone marrow.

ORIGIN. Three theories of origin are proposed. (1) Inclusion of embryonal rests, presumably of primitive mesenchyme which is the first hematopoietic tissue; this may subsequently produce nodules of marrow and even of bone. (2) Embolism of marrow cells through the blood stream. (3) Metaplasia of cells, especially reticulo-endothelial cells of the blood capillaries and sinuses.

CLINICAL FEATURES. None. This is an infrequent incidental observation at autopsy. It is not a manifestation of extramedullary hematopoiesis in blood dyscrasias.

DESCRIPTION. Usually, there is a single mass in one adrenal, but occasionally a single mass is also present in the opposite adrenal. It is spherical, ellipsoidal, or ovoid, with a dimension of from a few millimeters to 5 or 6 centimeters. The outline is fairly sharp, but the lesion is not encapsulated, except perhaps in rare instances. The color varies from pale yellow to bright yellow and from reddish brown to brown. The consistency is moderately firm. Hard foci of calcification or ossification are rarely observed.

MICROSCOPIC. The lesion is well defined and surrounded by adrenal tissue which is not likely to be compressed (fig. 6). Usually the principal component is fat in the form of large single vacuoles. Only rarely do immature fat cells with numerous small fat droplets occur. Between the fat cells are cells like those of bone marrow. These may be in small foci which require careful search for identification, or the marrow cells may be in great abundance. There is much variation from lesion to lesion. In some instances, cells of the granulocytic series preponderate, while elsewhere the principal cells are of the erythrocytic series. Lymphocytes are often present and occasionally megakaryocytes. Mitotic figures have not been reported. The lesion is usually rich in capillaries. Fibrous stroma is usually scanty but may be abundant. In none of our cases has a capsule been present.

DIFFERENTIAL DIAGNOSIS. The rare adrenal lipoma is not encapsulated and is not well vascularized. It is devoid of cells of bone marrow. It is possible that growth of bone may give the appearance of osteoma, but marrow is also present.

Reference

Giffen, H. K. Myelolipoma of the adrenals. Report of seven cases. Am. J. Path., 23: 613–625, 1947.

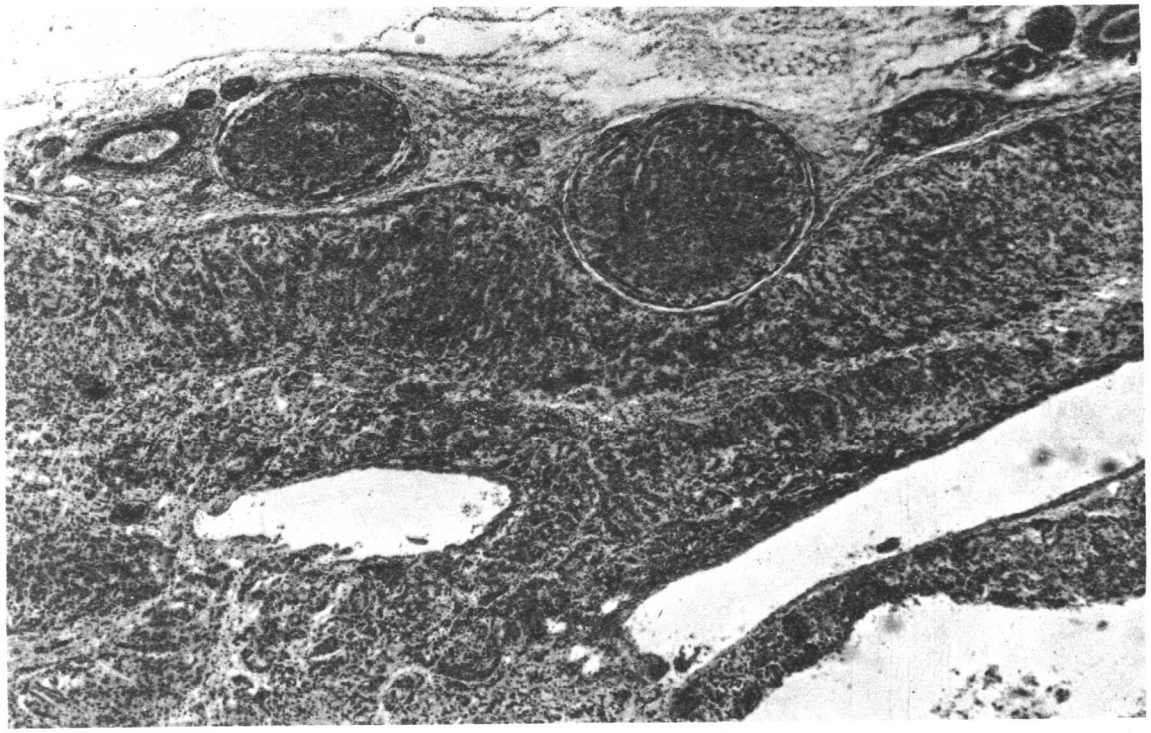

Figure 1. Cortical nodules in and outside capsule of adrenal. × 53. A. F. I. P. Neg. Acc. No. 218755–1.

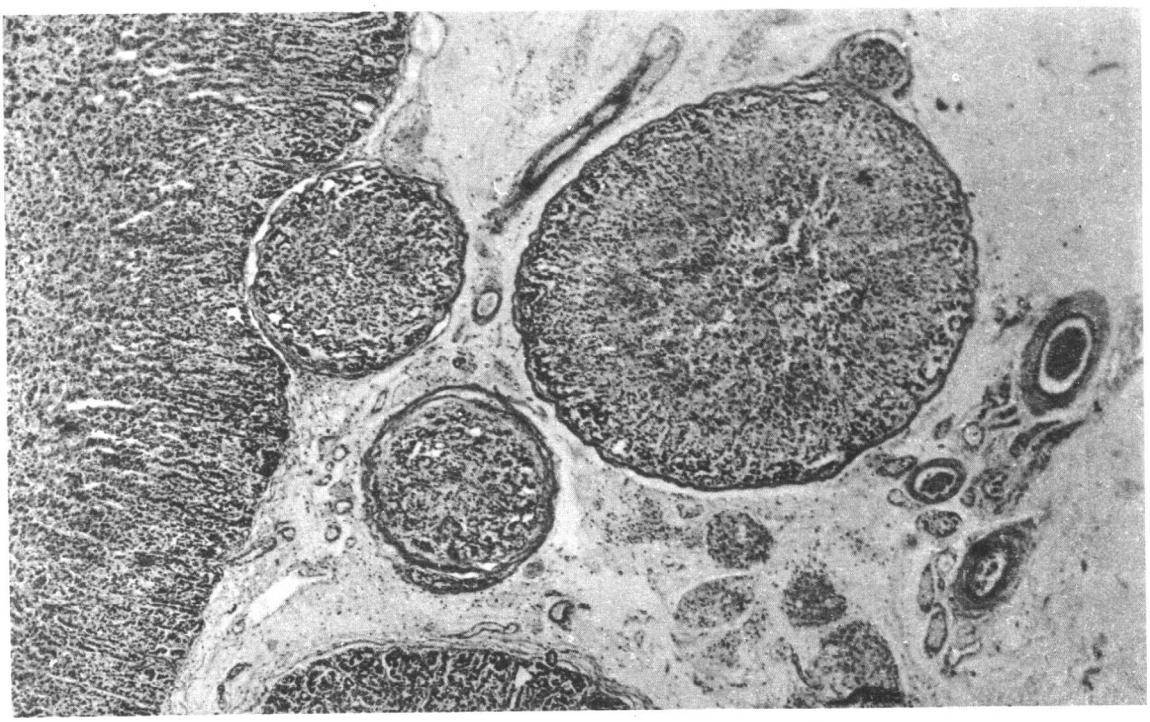

Figure 2. Cortical nodules outside capsule and in periadrenal fat—only apparently isolated from cortex. × 53. A. F. I. P. Neg. Acc. No. 218755–2.

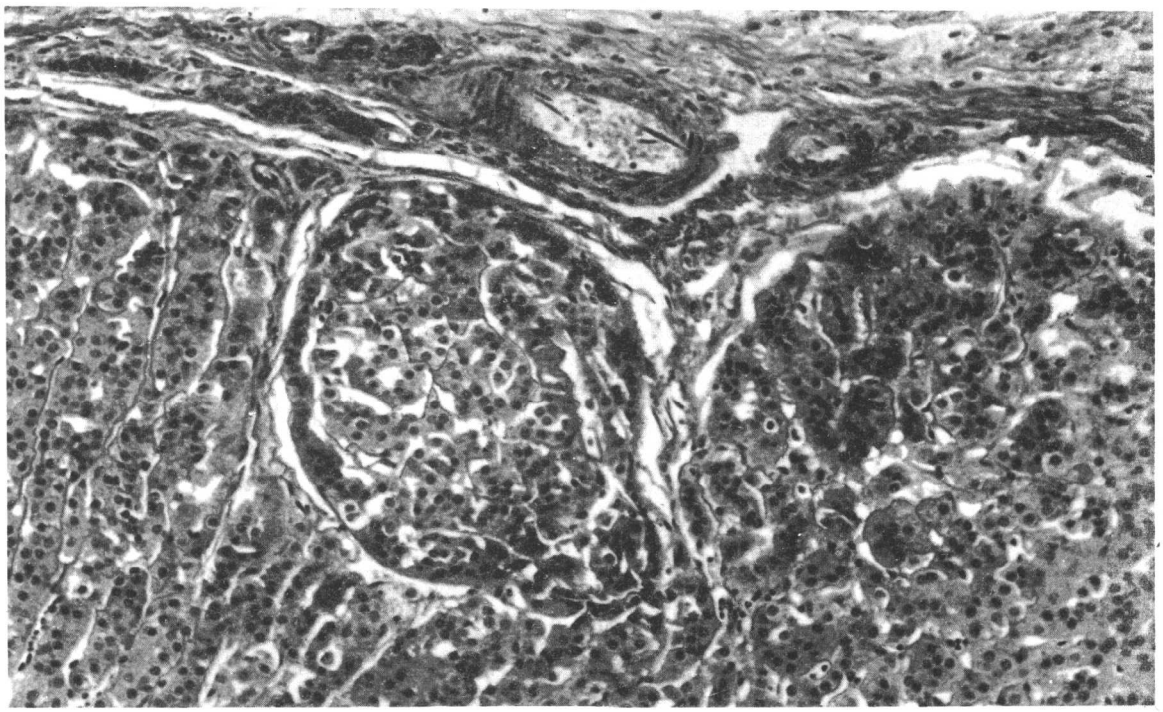

Fig. 3

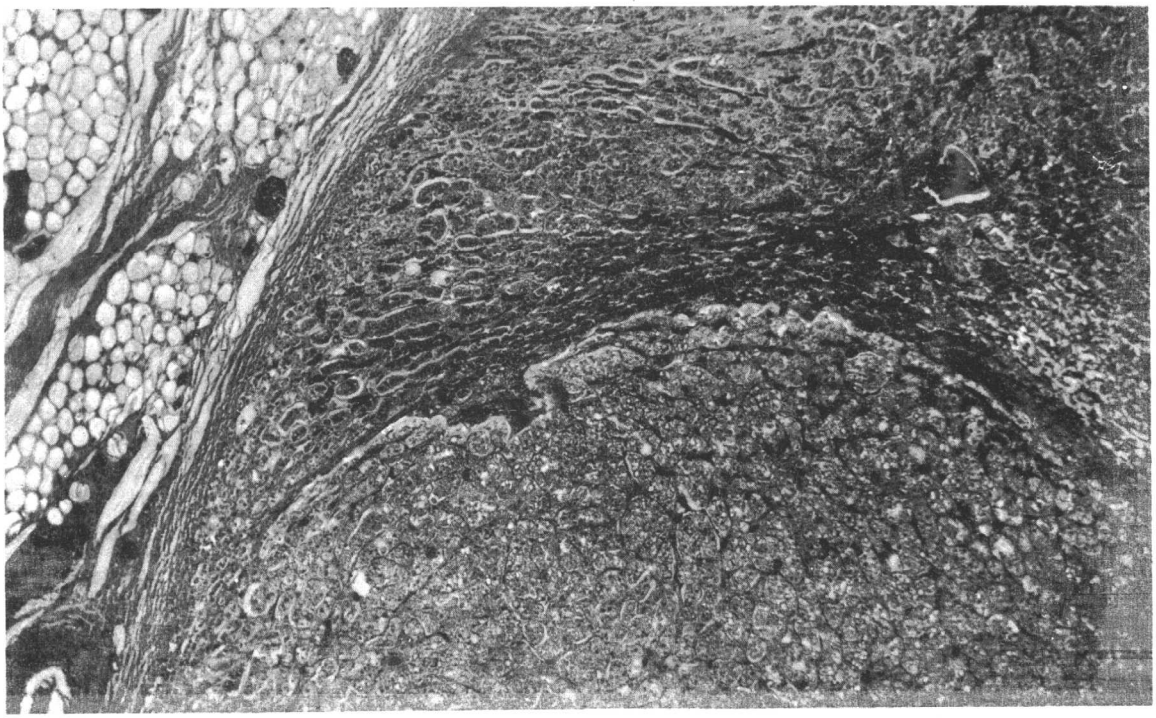

Fig. 4

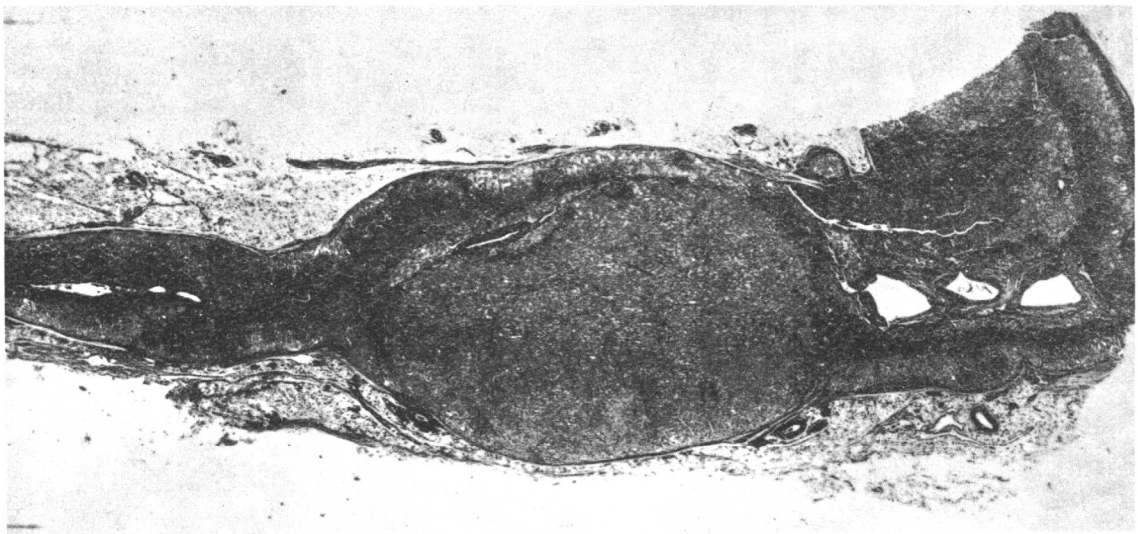

Fig. 5

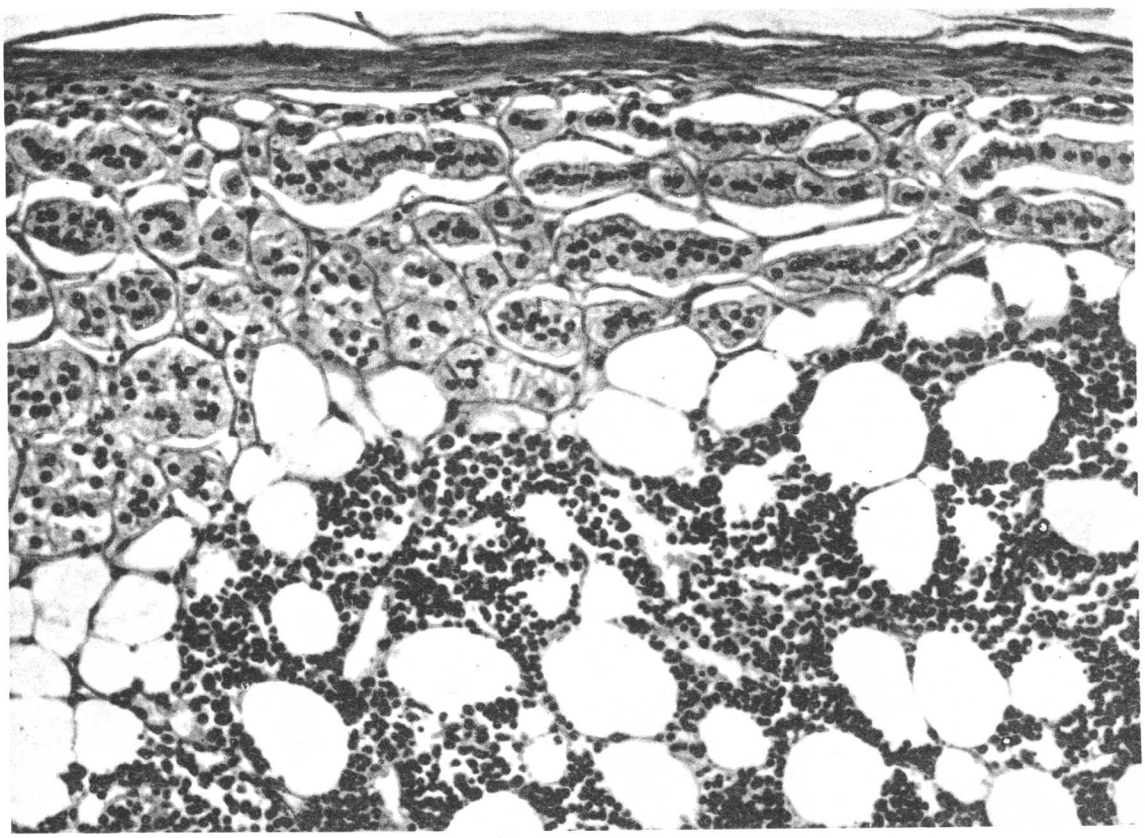

Fig. 6

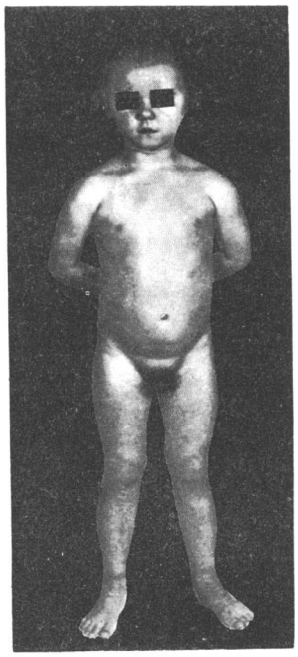

Fig. 7

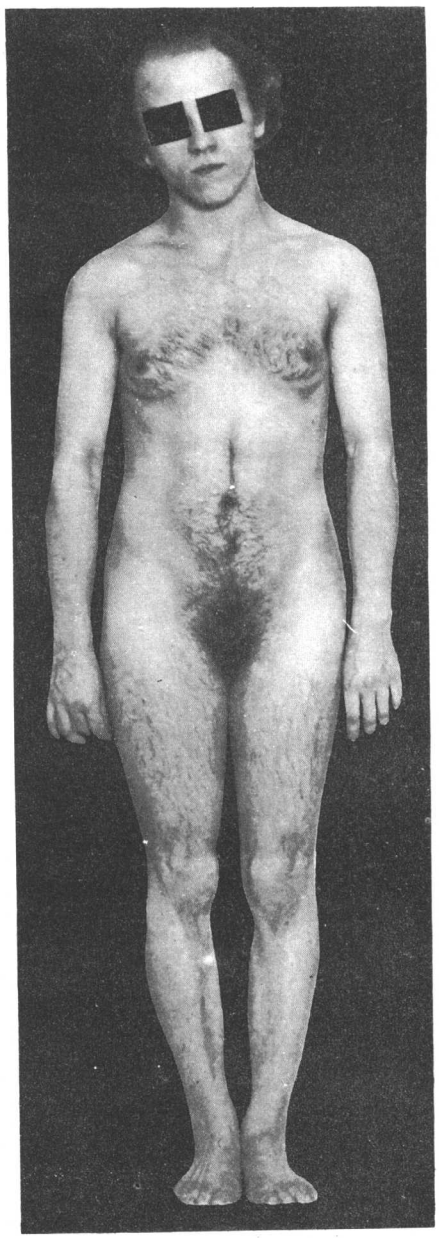

Fig. 8

Fig. 9

HOMOLOGOUS TUMORS

CORTICAL TUMORS

Cortical Adenoma. Synonyms and Related Terms: Adenoma substantiae corticalis suprarenalis (Lat.); adenoma; adrenal hypernephroma; functioning cortical tumor; granular cell tumor of adrenal cortex (Cahill).

DEFINITION. Cortical adenomas are benign encapsulated neoplasms composed principally of cells resembling those of the adrenal cortex. They are usually single and unilateral, of variable size, but sometimes exceedingly large. The term "adenoma" is used because of the origin in a gland; only rarely are acinic structures evident.

ORIGIN. There is no proof that the tumor is derived from mature cortical cells. The variable cellular picture can be explained by an irregular progression of the usual change from the zona glomerulosa through the fasciculata to the reticularis. However, the tumor may originate in primitive cells which have the potentiality of this progression. It is also possible, but not proved, that a cortical nodule may give rise to an adenoma.

CLINICAL FEATURES. In early life, the lesion is more frequent in females, but this difference is not so great in adult life. The tumor may occur from infancy to late adult life, but is most frequent in childhood and adolescence. Functional alterations are more common in early than in later life and may be absent in adults. The clinical manifestations depend on (1) the size and position of the tumor, (2) the production of hormones by the tumor, and (3) the metabolic disturbances incident to hormonal activity.

The tumor may be large enough to produce bulging of the flank or general enlargement of the abdomen. Tumors of lesser size may be palpable. Pain is infrequent.

HORMONAL PHENOMENA are included in the term adrenogenital syndrome and are conditioned by age and sex. Adrenal cortical dysfunction can occur in benign or malignant tumors and may also be present without neoplasia, due either to hyperplasia, or to hyperfunction of an organ, the size of which is not necessarily increased. Developing in utero, the tumor may be accompanied by female pseudohermaphroditism, but more often there is only cortical hyperplasia in these patients. The sexual properties of the adrenal cortex are indicated by virilism of girls, somatic sexual precocity of boys, and, rarely, feminism of men and boys.

In young patients of either sex, bones may grow rapidly with increased length of long bones, advanced bone age terminating in premature closure of the epiphyses. Such arrest of the growth of the long bones while the trunk continues to increase in length produces a resemblance to achondroplastic dwarfism. Premature dentition also occurs. Slight degrees of persistent or periodic hypertension may occur but without those symptoms attributed to excess release of epinephrine which occur in cases of pheochromocytoma.

Virilization of females varies with age. In children, secondary sexual characters develop, including enlargement of mammary glands, mons pubis, labia and clitoris, growth of hair on pubis and axillae and sometimes on face, deepening of voice, advanced bone age, and acceleration of growth (figs. 7, 10, 11, 12, 13). Between menarche and menopause, especially near the former, fat distribution is like that of males with broad shoulders and narrow hips, small breasts, conspicuous hirsutism (fig. 8) of the body, male type of escutcheon, deep voice, seeming enlargement of larynx, large clitoris sometimes erectile, and amenorrhea or reduced menstrual flow. Libido may be normal, reduced, or inverted. When hormonal activity occurs in the postmenstrual period, the principal changes are hirsutism, enlarged clitoris, deep voice, and sometimes minor psychic disturbances. Of the 70 cases (53 girls and 17 boys) which were collected by Wilkins, changes resembled those of Cushing's syndrome in 41 percent (22 cases) of girls and in 12 percent (2 cases) of boys.

In boys there may be precocious development of sexual characters, principally somatic. There is vigorous growth of hair on the head, face, and body, accompanied by macrogenitosomia praecox, and a deep voice (figs. 10, 11, 12, 13). Erections occur and emissions have been reported. Broster and Patterson report that in heterosexual virilism the patient has two adrenal glands, but in isosexual virilism there may be complete absence of one adrenal.

Feminization of males has been reported in 12 instances. All were in patients between 26 and 44 years of age except one at 5 years and one at 15 years. The usual clinical manifestation is gynecomastia. In some there is also atrophy of testes, and in some a reduction of libido and potency. As might be expected with cortical tumors of later life, many of these proved to be carcinomas.

Acne is frequent in boys and girls. Muscular development of the "infant Hercules" types is not frequent and is more often observed in girls than boys (figs. 7, 10).

Urinary hormonal assays do not give constant results. In virilized females, androgens are usually increased in amounts. The 17-ketosteroids may be as much as 50 times the normal. However, the assays may give figures in the upper range of normal. Sometimes the amount of pregnanediol is also increased, indicative of production of progesterone by the adrenal tumor. Probably the most significant androgen is dehydroisoandrosterone. When it

and associated steroids are present in excess, the diagnosis of cortical tumor is assured by the analysis of urinary steroids. Broster and Patterson describe a simplified test of these steroids. The test is of considerable value in distinguishing those cases of Cushing's syndrome associated with cortical hyperplasia of the adrenal, with or without basophilic adenoma of the pituitary, from those in which there is adrenal cortical tumor. In the hyperplasias the dehydroisoandrosterone is not in excess, whereas in the cortical tumors it is increased.

The figures for estrogens in virilized cases are variable, but approximately within normal range. In the few assayed cases of feminization, the estrogen output is variable, but in a few cases there has been a large increase in output of estrogens together with a slight increase of androgens.

Metabolic changes reported include those of fat, carbohydrate, and protein. Obesity is rare except in those cases with Cushing's syndrome. Obesity should not be confused with enlargement of abdomen by tumor or protrusion because of osteoporosis. Glycosuria and diabetes occur with adrenal cortical tumors but are noted especially in those cases with Cushing's syndrome. Evidence implicates adrenal steroids.

Patients with cortical hyperfunction may have a negative or a positive nitrogen balance. This appears to account in part for the marked clinical variations, particularly in that some cases show muscular atrophy and others hypertrophy (figs. 12, 13). Albright * explains the alterations in nitrogen balance as due to variability in production of "S" (sugar) and "N" (nitrogen) steroid hormones. The "S" hormone, being "anti-anabolic" inhibits synthesis of tissue and when present in excess, as in Cushing's syndrome, results in a negative nitrogen balance, cessation of epiphyseal growth, and neutralization of the pituitary growth hormone. The low level of tissue growth is little changed by high protein diet. In addition, the 11-ketosteroid urinary excretion is increased, and hyperglycemia may be present. The "N" hormone action is similar to that of testosterone and stimulates tissue growth, thereby producing a positive balance of nitrogen, calcium, phosphorus, and potassium, as well as increased growth, excessive sexual and somatic development, and marked virilism. It also causes an increase of 17-ketosteroid excretion.

Cortical extracts of the desoxycorticosterone type also play a role in the maintenance of water-sodium level of the body. Destruction of cortical tissue, whether from Addison's disease, hemorrhage, bilateral tumors, or tumor with contralateral atrophy or other causes, results in low plasma sodium chloride, dehydration, hemoconcentration, low blood pressure, and shock. Conversely, when desoxycorticosterone is increased, as occurs in some of the functioning cortical tumors (Conn), the sodium and chloride content of plasma, urine and sweat is increased, and blood pressure tends to rise. In general the potassium level is inverse to, but does not closely parallel, that of sodium.

*Albright, Fuller, Personal Communication.