SUPRARENAL TUMORS

CHARLES F. GESCHICKTER, M.D. 2

(From the Surgical Pathological Laboratory, Department of Surgery, Johns Hopkins Hospital and University)

A variety of neoplasms arising in the suprarenal gland have been described. Primary tumors of this organ are of two types, cortical and medullary. The cortical tissue is derived from mesoderm and is closely associated with the gonads and urogenital cell mass. The chro-

Fig. 1. Section of normal adrenal gland showing the characteristic arrangement of cortical and medullary tissue. Path. No. 47384

maffin cells of the medulla, on the other hand, are derived from primitive neural elements having an origin in common with other components of the sympathetic nervous system. The pathologic behavior of the tumors emphasizes this two-fold origin (Fig. 1). The more rapidly growing cortical tumors are accompanied by changes in the sex characteristics of the patient, while the medullary tumors show a variety

1 No reference is made in this article to the so-called hypernephromas occurring in the kidney, liver, or glands. In the author's opinion the hypernephromas of the kidney are true renal carcinomas and have been discussed in a previous article (Geschickter, C. F., and Widdershorn, H.: Nephrogenic Tumors, Am. J. Cancer 22: 620, 1934). Adrenal cortical tissue has not been observed in the liver or gonads in the material on file at the Johns Hopkins Hospital. Metastatic cancer in the suprarenals has been discussed in a previous article appearing in this Journal (Burke, E. M.: Tumors of the Adrenals, Am. J. Cancer 20: 338, 1934).

2 Aided by a grant from The Anna Fuller Fund.
of microscopic structures similar to neurogenic tumors of the sympathetic system. The present paper is based upon 105 cortical and medullary suprarenal tumors on file in the Johns Hopkins Hospital. Both groups of tumors throw important light on the endocrine functions of the suprarenal gland.

**Benign Cortical Tumors**

Cortical tumors may be classified as benign or malignant from the pathologic standpoint and as symptomatic or asymptomatic from a clinical point of view (Table I). The majority of cortical tumors in

<table>
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<th>Table I: Suprarenal Tumors</th>
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<tr>
<td><strong>Cortical Tumors</strong></td>
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<tr>
<td><strong>Benign Adenomas</strong></td>
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<td>A. Asymptomatic</td>
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<td><strong>Malignant Tumors</strong></td>
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<td>Female adult—hirsutism</td>
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| Medullary Tumors          |
| (33 cases)                |
| Neuroblastomas, malignant |
| Children                  | 17 cases |
| Adults                    | 6        |
| Paragangliomas, malignant and benign | 8 |
| Ganglioneuromas, benign   | 1        |
| Chromaffin tumors, benign | 1        |

this series and in the literature are benign, asymptomatic lesions discovered at autopsy (Figs. 2 and 3). The cell mass may be inconspicuous and regarded as a localized hyperplasia of the cortex, or there may be a definite neoplasm of mottled brown or yellow, approaching in size an adult fist. In a series of 66 cortical adenomas or localized hyperplasias studied in this series, only 3 produced clinical manifestations. In one of these cases the syndrome was of a definite endocrine nature.

Microscopically, the benign tumors are composed of a disorderly arrangement of cortical cells, rarely showing the order of zones found in the normal cortex. Many of the cells have a high lipid content. Masses of such lipoidal cells with degenerating cytoplasm and small dense nuclei are seen surrounding a capillary network. Other cells of
the cortical type may grow in cord-like, glomerular, or reticular arrangement, recalling the zones of the normal suprarenal cortex. These cells have a definite amount of clear cytoplasm. The nuclei are dense, may be fairly large, and are asymmetrically located. Deposits of chromaffin pigment are common. The distinguishing characteristics of cortical adenomas are the definite cortical cells, the tendency to lipoidal degeneration, the marked capillary network, the pigment deposits and the arrangement of the cells in cords or bundles (Figs. 2 and 3).

Both sexual precocity in children and virilism (pseudohermaphroditism) in adults have been described in the literature as occurring in patients with benign adenoma or hyperplasia of the suprarenal cortex.

Recently Lightwood (1) reported a cortical adenoma in a male infant of eighteen weeks who showed hypertrichosis and an accumulation of fat about the face, but no other sexual disturbances.

In a patient whose adrenals were explored by Dr. H. Young, and who was studied in the Harriet Lane Home on the service of Dr. E. A. Park, there was hypertrophy of the right adrenal but no definite tumor formation. The patient at the time of admission was four years of age and had shown precocity since the age of four months. He began to talk at fourteen months in a deep voice. At the age of two his penis was larger than normal, erections were frequent, and the child’s strength was such that he could overpower children of seven and eight years. At the age of four he had a definite mustache and a markedly muscular torso; his weight was 7 kilos beyond the predicted value, and the penis measured four inches (Fig. 4). There were evidences of rickets and mental retardation. The blood pressure was slightly elevated, 130/80. The white blood cell count was 11,800, with 70 per cent lymphocytes. There was a prolonged rise of the blood sugar after glucose injections, showing decreased sugar tolerance. The epiphysial development of the bones was that of puberty. The Aschheim-Zondek and Friedman tests on the urine were negative (Fig. 4).
In another case of an adult aged fifty, dying in uremia, autopsy disclosed a cortical tumor of the adrenal measuring $3 \times 2 \times 2$ cm. (Fig. 5). It is doubtful whether the elevated blood pressure in this instance (250/180) could be related to the adrenal tumor.

**Malignant Cortical Tumors**

Malignant tumors of the suprarenal cortex are rare. Unlike the benign adenomas, they are accompanied by pronounced endocrine disturbances. The sex changes are referred to collectively as the suprarenal-genital syndrome (Gallais, 2), and are of two types according to the age of the patient. In children sexual precocity occurs and in adults sexual inversion. Both sexes are affected, but females far more commonly than males. Endocrine disturbances outside of the sexual sphere are not uncommon. Adiposity, disturbances in sugar metabolism, skeletal changes, and polycythemia are recorded with carcinoma of the adrenal cortex. In children mental retardation is observed, and in adults psychic disturbances may be noted. Positive reactions for both the pituitary sex hormone (Aschheim-Zondek test) and the female sex hormone (Allen-Doisy test) may be obtained on the urine of these patients.

**Sexual Precocity:** Gordon and Browder (3), reporting sexual precocity in a boy of three with suprarenal carcinoma, were able in 1927 to find 23 similar cases in the literature, 19 occurring in girls and 4 in boys. Although no case of pubertas praecox associated with a malig-
nant tumor of the adrenal occurred in the series reported here, 5 additional cases have been found in the literature, bringing the total to 31. In female children the development of the breasts is marked, menstruation occurs, and the uterus and ovaries become enlarged, the latter showing definite corpora lutea. The patients increase rapidly in height and weight. The clitoris is enlarged and there is a tendency toward a profuse growth of hair on the lip and chin, and in the axillae and pubic region.

**Fig. 4. Precocious Puberty Occurring in a Boy of Four Years, Associated with Hyperplasia of the Right Adrenal Cortex. H. L. H. No. 81794**

(Courtesy of Dr. E. A. Park)

In males the clinical picture resembles that already described under benign adenoma (Fig. 4). These patients are herculean in build, with enlargement of the external genitalia, and a beard and mustache, with the growth of pubic and axillary hair. In boys no inversion of the sex characteristics is noted, but in girls there is a definite tendency in this direction.

**Sexual Inversion:** In adult females the genital-suprarenal syndrome takes the form described as hirsutism. Cases of this type have been recorded with some frequency in the literature and according to Collett (4) two such cases in married women were described by Hippocrates. The manifestations include hypertrichosis, with growth of a mustache and beard, a masculine voice, obesity, and cessation of menstruation.
The cells surround vascular spaces, have small dense nuclei and show lipoid degeneration in their cytoplasm. Case of Dr. F. W. Light.

The tumor affected both adrenals and was of ten years' duration. There were hirsutism and hypertrophy of the clitoris. Menstruation ceased at the age of twenty-four. Courtesy of Dr. G. Hunner.
In younger women there is a marked growth of the clitoris with a tendency toward pseudohermaphroditism.

The records of two such cases are available to us. One patient, twenty-eight years old, had been twice operated upon for adrenal tumors. The first was removed ten years previously from the right side. Five years later a tumor appeared in the left side and was explored by a surgeon elsewhere, but no tissue was removed. The second tumor continued to grow in spite of irradiation. The patient was of small stature, with an abundance of hair on the lip, face, and chest. The skin was coarse and there was eczema on the face. The breasts were flabby and atrophic, the uterus and cervix were small. The escutcheon was of the male type and the clitoris hypertrophied. The menses had ceased about four years previously. At the time of the third operation the entire pelvis was filled with a mass which was found on operation to be adherent to the abdominal wall and bowel. The tumor contained a large cyst with necrotic material. This was removed along with the tube and ovary on the left side of the uterus. Death occurred post-operatively, and it is probable that the second adrenal was removed with the mass (Fig. 6).

The second case has been previously reported by the author (5). It occurred in a woman of fifty-seven who suffered with edema, marked virilism, and hypertension (190/88). There was destruction of the
fifth thoracic vertebra, thought to be of metastatic origin, and areas of destruction were present in the femur. The patient died with a terminal infection resembling erysipelas. The left suprarenal was replaced by a tumor approximately 10 cm. in diameter. The right suprarenal was atrophic. Metastases were present in the liver and bones (Figs. 7 and 8).

In male adults with malignant tumors of the suprarenal cortex, sexual inversion may occur, but is extremely rare. Holl (6) has reported two cases in males with gynecomastia in which the adrenal tumor was verified by microscopic examination. The first patient was a boy of fifteen years with a large tumor in the right upper abdomen. The pubic hair was of the feminine type; both breasts were enlarged and the nipples pigmented. Pigmented striae were present on the abdomen, as in pregnancy. In the second patient, a man of forty-four, enlargement of the breasts and pigmentation of the nipples were accompanied by pain. The testicles and penis decreased in size, and sexual feelings were lost. The patient gained in weight and the masculine character of the face disappeared (Fig. 9). The tumor, which was situated over the left kidney, was removed at operation, after which there was a return of the normal male characteristics.

Mathias (7) reported a similar case and one was described by Bittorf (8). Zum Busch (9) reported a case of carcinoma of the adrenal cortex in a man aged twenty-seven, with gynecomastia and lactation.

While sexual changes are common with malignant suprarenal tumors, none of the adult males and females in this series showed sexual changes with such neoplasms (Fig. 10).
Three explanations of the sexual changes observed with adrenal cortical tumors are found in the literature (Collett): (1) The adrenal cells of the tumor act indirectly on the gonads. (2) The adrenal cells retain their primitive sex functions and produce these changes. (3) The adrenal cells stimulate the anterior lobe of the pituitary, which in turn acts on the gonads. A review of the evidence favors a combination of the latter two explanations.

With rare exceptions, undifferentiated cortical tissue such as is found in benign hyperplasia of infants or in malignant tumors is associated with the genital-suprarenal syndromes. These changes are nota-

![Image](image-url.com)

**Fig. 9. Gynecomastia and Feminization in a Man of Forty-four Years with Carcinoma of the Suprarenal Cortex**

The tumor was successfully removed, after which the patient regained his masculinity. Case of Dr. G. Holl. Illustration from Deutsche Ztschr. f. Chir. 226: 277 ff., 1930.

bly lacking in benign cortical adenomas in adults containing well differentiated adrenal tissue. The origin of the suprarenal cortex from the genital ridge relates these undifferentiated cells in the embryo to the gonocytes. If the explanation of Krabbe (10) is accepted, that the testis takes its origin directly from such undifferentiated tissue, while the ovary represents a more highly differentiated structure, then the adrenal cortical tissue in its more primitive state is identical with testicular tissue. On the other hand, Moehlig (11) has accumulated evidence to show that hyperactive states of the adrenal cortex are associated with or stimulate a corresponding hyperactivity in the anterior lobe of the pituitary (Fig. 11).

In the genital-suprarenal syndrome, therefore, one would expect to find increased hormonal secretion of testicular and hypophyseal origin. Since both male and female sex hormones are excreted by testicular tissue (Laqueur, 12), increased outputs of the male sex hormone (androit), the female sex hormone (oestrin), and the anterior pituitary sex hormone (prolan A) are to be expected. Frank (13) has reported two cortical adrenal tumors with excretion of female sex hormone in the urine, and Copeland (14) has reported a probable case with prolan A
in high concentration in the urine. Tests for the male sex hormone have not been made to the writer’s knowledge.

Associated Endocrinopathies: Two other types of endocrine disturbances associated with adrenal cortical tumors deserve emphasis. Both of these may be associated with the genital-adrenal syndrome. The first is the so-called Cushing or Dercum syndrome, sometimes observed with basophilic adenomas of the hypophysis and accompanied by polycythemia. Polycythemia has also been reported with cortical tumors in the absence of the Cushing syndrome. The second is disturbance in the carbohydrate metabolism.

![Figure 10](image)

**Figure 10. Asymptomatic Carcinoma of the Adrenal Cortex Occurring in an Obese White Man of Fifty-five Years. Path. No. 7079**

The primary tumor was in the left adrenal, with metastases to the right adrenal, lungs, and gastro-intestinal tract. The patient was treated for ureteral calculi and hydrenephrosis.

In Frank’s cases, referred to above, the typical Cushing syndrome was present, characterized by obesity of the face and trunk, hirsutism, so-called pig eyes, persistently high blood pressure, with attacks of hypertension, amenorrhea and menstrual irregularity, pinkish skin striae, rarefaction in the bones, polycythemia, cyanosis of the extremities, and susceptibility to infection. Large carcinomas of the adrenal cortex but no pituitary adenomas were demonstrated. Zucker (15) has reported a case of a cortical carcinoma with polycythemia of 10,500,000 blood cells and a blood pressure of 145/95. The patient was a woman of thirty-five years with a growth of hair on the body and upper lip beginning five years previously, headaches, a deep voice, increase of weight and cessation of menstruation one and one-half years previously. Zucker cites two similar cases from the literature.
Disturbances in carbohydrate metabolism may be prominent. Anderson (16) has reported a case of fatal hypoglycemia associated with adrenal cortical carcinoma and has kindly submitted the microscopic material for study (Fig. 12). The patient was a male aged thirty-three, who had attacks of unconsciousness and diplopia with dimness of vision. Examination in April 1929 showed increased respirations, numerous furuncles, and mental confusion. The blood pressure was 120/80. Roentgen examination of the skull showed no pituitary abnormality. The optic discs were extremely pale, the blood sugar varied between 70 and 80 mg. per 100 c.c. The patient improved on glucose therapy. In July 1929, coma ensued, and the blood sugar fell to 60 mg. per 100 c.c. In spite of adrenalin and glucose administration, death followed. At autopsy the left adrenal gland was found to be replaced by a tumor 8 cm. in diameter. The right adrenal was smaller than normal. The pancreas and the pituitary were vascular. No other lesions or metastases were found. There are no other cases of this type recorded in the literature to our knowledge. Zucker's case showed increased sugar tolerance. In two cases in this series there was decrease in sugar tolerance, which is the most common finding recorded in the literature. Moore (17) has recorded a case of diabetes refractory to insulin which at autopsy showed hyperplasia and adenomatous nodules in the adrenal.

The pathological physiology of these endocrine disturbances is relatively obscure. While the undifferentiated cells of the adrenal cortex correspond in function to testicular tissue, the adult cells play a rôle in carbohydrate metabolism corresponding in kind, if not degree, to the insular tissue of the pancreas (Goldzieher, 18). When these adult cells are replaced by undifferentiated gonadal tissue, as in hyperplasia of infancy or cortical carcinoma in adults, decreased sugar tolerance and glycosuria may result. On the other hand, with more
slowly growing cortical tumors, hyperfunction of adult cortical tissue may lead to hypoglycemia and increased sugar tolerance.

Adrenal cortical tumors affect the fat metabolism both directly and indirectly. With increased secretory activity of these cells fat is stored in the tissues and removed from the blood (Goldzieher, 18). Part of this fat is probably stored in the muscles as glycogen, explaining the increased muscular strength of the patients. The adrenal cortical tissue also acts to suppress thyroid function, which would enhance obesity. In one of the cases in this series there was decrease in the basal metabolic rate (Fig. 7), the initial impression recorded being that of myxedema.

The adrenal cortex is intimately related to the oxygen functions of the blood and hence to the red cell count. This is the explanation usually given for the hypertrophy of the adrenals occurring in the fetus before the pulmonary circulation is established. The polycythemia observed with cortical tumors of the adrenal may be dependent, therefore, upon the increase in the amount of functioning cortical tissue.

**Tumors of the Adrenal Medulla**

Medullary tumors of the suprarenal show a variety of types, corresponding to those occurring elsewhere in the sympathetic nervous system. These tumors may be exceedingly malignant or benign, depending upon the degree of differentiation. The growths apparently arise from a single stem cell which wanders out from the neural crest in the first few days of embryonic life. Passing from the least to the most highly differentiated, the major groups are neuroblastomas, paragangliomas, and ganglioneuromas and chromaffin tumors. The last
two groups are equally differentiated, the ganglioneuromas represent-
ing the end-stages of neural differentiation, the chromaffin tumor re-
representing the end-stages of endocrine differentiation.

Neuroblastomas

The tumor occurring most frequently in the suprarenal medulla
arises during the early stages of development and shows a mass of
undifferentiated cells referred to as neuroblasts or sympathoblasts.
These tumors are usually seen in patients under the age of three years,
are rapidly fatal, and metastasize to the liver, lymph nodes, bones, eyes,
lungs, and other organs. Scott, Oliver and Oliver (19) have recently
reviewed the literature of these growths, bringing the total number
of cases to 162. In their structure these tumors resemble closely symp-
pathetic tumors occurring in the outlying vertebral ganglia, and also
other primitive neurogenic tumors common in children, namely retino-
blastomas and the medulloblastomas of the cerebellum.

The most common findings in the 17 cases in children in this series
were an abdominal mass accompanied by pain or vomiting and emaciation.
In adults vertebral metastasis may produce the initial symptoms.
Fever, exophthalmos, and joint pain are occasionally present in the
juvenile cases. With abdominal symptoms the initial impression may
be that of appendiceal abscess. Three cases in this series were op-
erated upon with this diagnosis. With fever and joint symptoms a
diagnosis of rheumatic fever may be suggested. This was observed
in a case reported by Frew (20). While fever is rarely noted in the
history, the majority of these patients show some elevation of tem-
perature during their course in the hospital.

Associated with the primary mass, one major group of cases (known
as the Pepper type) will show enlargement of the liver caused by
metastasis to that organ. In another group of cases metastases to the
bones, regional lymph nodes, and exophthalmos are the outstanding
findings, constituting the so-called Hutchison syndrome.

Pepper's (21) original contribution emphasized the early age at
which the tumor appears (three to eleven weeks), the rapidly fatal
course, and the enlargement of the liver without ascites or jaundice.
The younger age of the patients showing the Pepper type of adrenal
neuroblastoma may account for the more rapid and invasive course
of the tumor. Since the adrenals are in immediate contact with the
liver, these more malignant growths tend to invade that organ by
direct extension or via the anastomosing superficial vessels.

Hutchison (22) described "a definite clinical syndrome" in 10 cases
of suprarenal sarcoma with metastasis in the skull. All the patients
were children. "In the majority of the cases the first thing noticed
was some swelling about the bones of the skull . . . sometimes preced-
ing this, proptosis of one or both eyes was observed."

Observations in our own cases show an overlapping of the Pepper
and Hutchison syndromes. Where the bones are involved, there may
FIG. 13. ROENTGENOGRAM SHOWING A HUGE LIVER AND ASSOCIATED ABDOMINAL MASS IN THE PEPPER SYNDROME PRODUCED BY NEUROBLASTOMA OF THE SUPRARENAL GLAND WITH METASTASES TO THE LIVER. H. L. H. NO. 79311

FIG. 14. ROENTGENOGRAM OF BONE METASTASES IN THE HUTCHISON SYNDROME PRODUCED BY NEUROBLASTOMA OF THE SUPRARENAL GLAND WITH SKELETAL METASTASES. PATH. NO. 51971
also be abdominal enlargement due to metastases to the liver, and enlargement of the regional lymph nodes may occur in either type. While anemia is a more pronounced feature with the Hutchison syndrome, severe secondary anemia may also occur in the advanced stages of the Pepper type.

Although absence of ascites was considered by Pepper to be one of the prominent clinical features of his cases, ascites was present in two instances in this series when the abdominal cavity was opened at autopsy.

In cases of the Pepper type roentgenograms of the abdomen may show a diffuse mass clouding the affected side, overlapping the shadow

of the liver and elevating the diaphragm (Fig. 13). Pyelograms showed shifting of the pelvis in one case. Besides elevation of the diaphragm, x-ray films of the chest may show metastases in the lungs. However, pulmonary metastasis and involvement of the mediastinum by nodular masses are rare.

Involvement of the long bones, spine, or pelvis may be demonstrable roentgenographically before involvement of the skull in patients who eventually develop a Hutchison’s syndrome (Fig. 14). The metaphysial regions of the long bones show the earliest and most pronounced areas of resorption, which are characteristically wedge-shaped in appearance. A periosteal reaction may overlie the defect. The skull is involved in the region of the calvarium. Here the metastases produce minute foci of destruction resulting in a worm-eaten appearance.

Fig. 15. Typical Neuroblastoma of the Suprarenal Gland with Rosette Formation.
Path. No. 2216

The lesion occurred in an infant of eighteen months and metastasized to the liver and lungs. From Lewis and Geschickter: Arch. Surg. 28: 16, 1934.
Neuroblastomas, which may be solid or cystic, are composed of small cells with hyperchromatic nuclei and little cytoplasm. They are characteristically clumped. Rosettes were found in a little more than one-third of the cases in this series, although reported in the literature as occurring in 50 per cent of the cases (Fig. 15). The small cells usually referred to as sympathoblasts predominate in all cases where the tumor occurs in infancy. Larger cells with definite amounts of cytoplasm are more common in the rare cases occurring in adults (Figs. 16 and 17). Larger ganglion or chromaffin cells seen in benign ganglioneuromas or paragangliomas have been described in neuroblastomas but are rare.

**Figure 16. Photomicrograph of Neuroblastoma showing the characteristic clumping, the dense nuclei, scarcity of cytoplasm, and stroma of the tumor occurring in infants. Path. No. 47902**

Compare with Figure 17.

The clinical course in these cases is rapid and fatal. The tumors are not radiosensitive, and only one case of surgical cure has been reported (Lehman, 23).

**Paragangliomas**

In paragangliomas of the suprarenal glands, hypertension, hypotension, and vasomotor instability are not infrequently observed. Two of the patients reported with paraganglioma of the suprarenal presented Addison’s syndrome, one with fainting attacks and the other with melanoderma. In these cases the suprarenal cortex may be invaded and destroyed, but persistence of the cortex on one side had been noted. Among the varied clinical manifestations in addition to those already mentioned, may be noted multiple neurofibromatosis,
diabetes or glycosuria and lesions of the thyroid. In contrast to cortical tumors, which may be accompanied by hypothyroidism, these cases show hyperthyroid tendencies.

Eisenberg and Wallerstein (24) in a recent review of 50 paragangliomas reported in the literature came to the conclusion that there is no significant relationship between these chromaffin tumors and hypertension. The tumors occurred with equal frequency in the sexes. They appeared most frequently in the fifth decade, the age limits being two and a half and eighty-two years. According to these authors, only 5 of the reported tumors were malignant, and in all of these both suprarenal glands were involved. In the author’s series malignant tumors were as frequent as the benign growths.

FIG. 17. NEUROBLASTOMA OCCURRING IN AN ADULT. PATH. NO. 53560

The initial symptoms were caused by metastases to the lumbar vertebrae. The cells have a small but definite amount of cytoplasm. Compare with Fig. 16. Case of Dr. L. W. Larson.

Paragangliomas of the adrenal rarely reach a large size. The larger tumors are more often cystic than the small ones and the cyst contents are usually hemorrhagic. The smaller tumors are, as a rule, surrounded by a rim of compressed adrenal cortex. Histologically an alveolar arrangement of the cells is found in the benign growth, with a tendency to syncytial formation. The cells vary markedly in size, cuboidal and polyhedral forms of moderate size predominating. In the malignant tumors, giant atypical ganglion cells and large spindle cells may be found (Figs. 18 and 19). The epithelial cells, when freshly stained with chrome salts or when fixed in Zenker’s solution, show pigmented granules.

Chromaffin Tumors and Ganglieneuromas

The more highly differentiated tumors of the suprarenal medulla may be either neurogenic or chromaffin in character. The ganglieneuroma represents the most highly differentiated neurogenic tumor
Fig. 18. Benign Paraganglioma of the Medulla of the Suprarenal Gland Occurring in a White Woman, Aged Fifty-three, and Producing Symptoms Referable to the Kidney. Path. No. 46958

The patient has remained well following excision. From Lewis and Geschickter: Arch. Surg. 28: 16, 1934.

Fig. 19. Malignant Paraganglioma of the Suprarenal Gland Metastasizing to the Entire Skeleton, in a White Woman, Aged Sixty-five. Path. No. 54424

The photomicrograph was taken from a biopsy specimen from a large fungating lesion on the inferior alveolar margin. The patient died shortly thereafter.
and the chromaffinoma or chromaffin-cell carcinoma the most highly
developed endocrine tumor of the medulla. Both forms are rare but
both benign and malignant varieties of each have been described.

Ganglioneuromas are equally rare in the suprarenal gland and other
sympathetic structures. Including the cases collected by McFarland
(25) and Lewis and Geschickter (26), 111 have been reported to date
for the entire sympathetic system. The benign ganglioneuroma is
usually a small tumor found accidentally at autopsy within the medul-
lar substance of the suprarenal gland or occasionally overlying this
gland and arising from sympathetic structures at the hilus. Such
tumors are composed of a mass of fibrils enclosing occasional large

![Image of Ganglioneuroma](https://example.com/fig20.jpg)

**Fig. 20. Ganglioneuroma of the Retropertitoneal Spaces in a Girl Aged Fifteen.**
Path. No. 47692

In addition to the ganglionic and chromaffin cells shown, other portions of the tumor con-

ganglionic cells (Fig. 20). Less differentiated tumors of this group
show an increasing number of poorly developed ganglionic cells and
local invasiveness and may give rise to definite metastases.

Chromaffin-cell Tumors: Tumors of the chromaffin cells of the supra-
renal medulla are perhaps the rarest of the neoplasms involving this
organ. They occur uniformly in adults and are usually accidental
findings at autopsy. The growths are small and encapsulated. They
are a mottled suprarenal color (yellow-brown-red). They may be
bilateral. Malignant forms are rare.

In the malignant chromaffin-cell carcinomas the cells are large and
epithelial-like, grow in an alveolar arrangement or in sheets, and show
many bizarre nuclear forms and tumor giant cells. Diagnostic criteria
include absence of fat, lipoids, and glycogen in the cells, a positive
chrmatite reaction, and large, malignant, epithelial-like cells forming
synctial masses or tumor giant cells.

Only one case of chromaffin-cell tumor is recorded in the present
series. It was found in a white man aged forty, who apparently died
of antimony poisoning. At autopsy a tumor the size of a small orange
was found replacing the left suprarenal gland. No indications of the
tumor had been discovered during the life of the patient. The histol-
logic structure is shown in Fig. 21.

Endocrine manifestations with medullary tumors of the suprarenal
gland are less varied and less common than with cortical carcinoma.
Among the neuroblastomas, paragangliomas, ganglioneuromas and

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**Fig. 21. Chromaffinoma of the Medulla of the Suprarenal Gland with Large Syncyte-
tial Giant Cells. Path. No. 46650**

This tumor was found accidentally at autopsy and did not involve structures beyond the
medulla of the suprarenal gland. Although it was clinically benign, there were many nuclei

chromaffinomas just discussed, the paragangliomas are the only group
with marked endocrine disturbances. With these tumors variability
in the blood pressure is the most common finding. With rapid growth
and invasion of cortical tissue Addison’s disease may occur. Hyper-
glycemia and glycosuria dependent upon increased secretion of adrena-
lin occur. The hyperthyroid state with asthenia sometimes associated
with these medullary tumors is in marked contrast to the obesity,
hypothyroidism, and increased muscular efficiency seen with cortical
neoplasms.

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