of cases, however, the hæmorrhage causes sudden hypoadrenia. The treatment of this condition is that indicated in the emergency cases of terminal hypoadrenia (see page 113). If the hæmorrhage has not been too extensive the chances of recovery will be greatly increased by the use of adrenal or pituitary preparations, the latter owing its properties, in my opinion, to the adrenal chromaffin substance the pituitary contains.

ADRENAL HÆMATOMA.

(*Adrenal Hæmorrhagic Pseudocyst.*)

Adrenal hæmatoma, which usually develops in but one adrenal, occurs as a complication of the condition just reviewed. It becomes a source of fatal adrenal hæmorrhage when the cyst breaks and empties its contents into the abdominal cavity. It indicates that the form previously described is not always fatal, but also that the lesions left behind may serve as the initial lesion of another grave disorder. Especially does this apply when but one adrenal is the seat of hæmorrhage. Its original causes, when these are traceable, are the same as those of the acute form: acute intoxications, especially diphtheria, typhoid fever, burns, osteomyelitis, hepatic abscess and tuberculosis, atheroma of the adrenal arteries, thrombosis of the adrenal veins, traumatisms, etc.

Pathogenesis and Symptomatology.—While older investigators, including Klebs, Virchow, and Heuschen, considered these growths as retention cysts similar to those formed in the thyroid, and thus termed them "struma adrenalis," the prevailing view at the present time is that a small hæmatoma or an acute congestive process initiates the growth. As the latter increases in size, the adrenal structure is gradually destroyed and the contents is no longer—unless a recent hæmorrhage has occurred—merely blood, but a more or less fluid magma of detritus, broken-down blood- and tissue- cells, flakes of fibrin, cholesterin crystals, etc., which may be dirty yellow, greenish, or brownish in color. Microscopically the walls of the cyst, which vary from 1/16 to 1/8 inch in thickness, are composed of fibrous tissue; the inner aspect shows shreds or remnants of the adrenal cortex. Certain thickened portions of the capsule and what

semiorganized clots the cyst may contain may be found to contain small cysts and chalky deposits. These growths sometimes become very large—as large as an adult head in a case of Chiari's—and contain several pints of blood or liquefied blood and tissue elements.

The symptomatology of adrenal hæmatoma introduces but little, if anything, of the symptom-complex of adrenal insufficiency (hypoadrenia) or overactivity (hyperadrenia), since the functions of the organs are not affected materially—otherwise than by pressure in some instances—owing to the ample margin (eleven times the actual needs of adrenal tissue) left undisturbed. Adrenal hæmatoma may, in fact, give rise to no symptom other perhaps than a sensation of weight, until quite large, when pain supervenes. This is at first indefinite, though most marked in the region of the tumor, in the right or left loin, or in the upper portion of the abdomen and loin. The neuralgia-like pain due to pressure upon the adjoining sympathetic plexuses becomes increasingly severe, and radiates in various directions, especially toward the hip and thigh of the corresponding side, and is subject to exacerbations, which may be very severe, especially after meals. Epigastric pain and vomiting (the latter of which affords relief) occur in some cases, especially during these exacerbations of suffering.

The tumor may manifest itself, at first, merely by enlargement of the abdomen. The bulging then becomes more clearly defined on one side or the other (this variety of growth being almost invariably unilateral) under the lower ribs, which may be pushed outward if the growth is sufficiently large, or below their free border, *i.e.*, between them and the superior spine of the ilium. If the tumor, which grows downward and forward, is sufficiently below the ribs to be palpated, it is usually found globular, or oval, smooth and tense, though elastic, to the touch. Fluctuation may also be elicited. In some cases it is immovable under palpation, though it may, at first, follow the respiratory movements. Nor can it be grasped as is sometimes possible in renal tumors; if small the tumor is movable either upward or downward, but this mobility gradually decreases as the tumor develops. The growth is sometimes sensitive under pressure.

At first, several years perhaps, the patient may appear

normal in every other respect, be well nourished, ruddy, etc. With comparative suddenness, however, he begins to fail, losing flesh rapidly, all the other symptoms mentioned, to which dyspnœa and a sense of constriction about the chest is added, becoming more severe. If the cyst does not rupture, polyuria, hæmaturia, and even slight bronzing may appear. It is probable, however, that this train of phenomena is witnessed only in a very small proportion of cases, rupture and hæmorrhage, constituting the "adrenal hæmorrhage" in adults treated under the preceding heading, being the outcome in practically every instance. Here, however, the rupture is external, giving rise to peritoneal manifestations—if these have sufficient time to develop at all.

Diagnosis.—The symptomatology of adrenal cyst apart from the location of the tumor does not present, as just shown, very characteristic features. The location of the pain sometimes suggests intercostal neuralgia; but, inasmuch as pain occurs only when the growth is large, percussion and palpation will reveal the presence of a tumor. In neuralgia the pain is also apt to be localized, thus distinguishing it from the radiating pain of adrenal cyst. The sudden onset of severe pain may be taken for acute pancreatitis. The location of pain and tenderness in the upper left abdominal quadrant, the subnormal temperature, and the early lethal trend—death occurring sometimes within three days—clearly point to the latter disease. Pancreatic cyst is also differentiated by its location and its association with glycosuria, stearrhœa, and imperfect digestion of fats and albuminoids. Hydatid cyst of the liver, another source of confusion, is attended by the presence of biliary pigments in the urine, the appearance of cysts in the stools and vomited matter, and with obstruction phenomena. Cancer of the spleen may be recognized by the more nodular outline of the growth and the cachectic phenomena. Hydatid cyst of the spleen is usually associated with hydatid cysts elsewhere and may be accompanied by the presence of hooklets in the excretions. Puncture of the growth should be carefully avoided when there is any suspicion whatever that an adrenal blood-cyst is present. Renal cysts are more easily palpated bimanually, and are usually freely movable.

The sudden appearance of symptoms of severe internal hæmorrhage (the adrenal hæmorrhagic cyst having ruptured into the peritoneal cavity or the subperitoneal cellular tissue), *i.e.*, the acute abdominal pain and other phenomena of collapse, etc., of adrenal hæmorrhage with death within a few hours or days, may first reveal the existence of adrenal hæmatoma; but in most cases it develops sufficiently to produce the pressure symptoms just described.

Prognosis.—The fact that adrenal hæmorrhage is practically always unilateral, and that the loss of one adrenal does not compromise life, as does removal of both organs, makes it possible to remove the growth with safety. The frequent instances of severe collapse and shock that have followed these operations suggest that the operative prognosis cannot but be improved by resorting to those surgical procedures which will entail the least possible handling of the intraperitoneal organs and of the sympathetic ganglia, all of which are well known to produce shock readily by reflex action.

Treatment.—The cyst may be removed through either an abdominal or lumbar incision. In accord with M'Cosh's advice, which a review of the operative results recorded fully sustains, preference should be given to the lumbar incision. The approach is more direct; it avoids the handling of the intraperitoneal organs, which must necessarily take place if the tumor be reached through the abdominal incision, and it affords the most direct route for drainage. In the average case, an oblique incision from behind downward and forward below the last rib, which has been found most convenient for extirpation of the kidney and ureter, is as applicable here. If much space is needed it is safer to remove the last rib than, as some European surgeons have advised, to resort to the abdominal incision, which, as previously stated, entails considerable shock. The tumor is sometimes found so firmly adherent to the kidney that removal of this organ becomes necessary.

HYPERNEPHROMA.

This name has been given to tumors formerly considered as lipomata, adenomata, or myxomata, but shown by Grawitz, in 1883, to be developed from adrenal tissue, either within the adrenals themselves or in the kidneys, the walls of blood-vessels,

or other structures in which "adrenal rests" (fragments of misplaced adrenal tissue) or "aberrant adrenals" occur.

From my viewpoint, these so-called "adrenal rests"—found in 90 per cent. of all autopsies by Bayard Holmes, at least once a week by Grawitz in his autopsies, etc.—are not misplaced fragments of adrenal tissue; they belong normally to the kidney and many other organs, even though composed usually of cortical adrenal tissue. I have submitted the view[225] that what has been termed the internal secretion of the kidney is a product which differs in no way from that of the adrenals, and[226] that the kidney and the adrenals were governed by the same nervous structures, being thus closely linked functionally. Under the influence of centric impulses the so-called adrenal rests and the adrenals are both caused to increase their secretory activity and to enhance the intrinsic metabolism of the tissues they supply. In some instances "adrenal rests" are composed of both cortical substance and chromaffin substance found in all sympathetic structures by Kohn, Wiesel,[227] and others.

Hypernephromas are relatively common in the kidney, constituting, as shown by Albarran and Joubert, 17 per cent. of all renal tumors; they are much less frequently found in the adrenals proper or in other organs, such as the uterus, ovary, the broad ligament, etc. Microscopically, they present the typical characters of the adrenal cortex and closely, as a rule, invest vascular channels. These vessels and adjacent tissues usually contain a colloid material similar to that found in the thyroid, or secreted by the adrenals. They are benign at first and become troublesome—sometimes after many years—mainly on account of their size, which sometimes reaches that of a child's head, but the pressure they exert on surrounding structures, their tendency, even when benign, to metastasize in the lungs, bones, brain, give them their malignancy.

PATHOGENESIS AND SYMPTOMATOLOGY.—Before the local symptoms of the tumor appear—when any are clearly discernible—hypernephroma evokes phenomena which are diametrically opposed to those of Addison's disease, and which correspond

[225] Sajous: Monthly Cyclopædia, June and July, 1909.
[226] See p. 467, this volume.
[227] Wiesel: International Clinics, vol. ii. 15th series, 1905.

with increased nutrition and stimulation of growth such as that produced by thyroid preparations in cretinism.

The symptomatology varies considerably in different cases and suggests that several types exist which our present knowledge does not enable us to discriminate. Some of these exhibit such malignancy that they have been grouped in a separate class. Beginning with hypernephromas of the adrenals proper, we may have:—

Malignant Hypernephroma of the Adrenals.—This growth occurs as a rule between the first and eighth year, especially in girls of the latter age, and causes premature development, so marked in some instances that the child appears, as to size and development, twice or three times its true age. Owen Richards[228] reported a case in a girl of 7 years, who was as tall as a person at 20. The face, genitalia and pubis, and sometimes the whole body are covered with an abundant growth of hair, the external genitalia being as fully developed as in the adult. The body is obese, the appetite and thirst excessive although gastric disorders, including stubborn vomiting, are common. The skin may be swarthy or dark-hued as in a brunette, or coppery. The voice is sometimes harsh and deep. Such children are usually cross and sullen, unlike obese children in whom the obesity is due to deficient fat catabolism. These primary growths of the adrenals, which are usually observed in girls, are of slow development, and years usually elapse before metastasis and pressure phenomena—those which give the growth its malignancy—appear.

The abnormal growth of the child may suggest gigantism or acromegaly due to some disorder of the pituitary body, but the characteristic growth of the extremities, the absence of obesity in these disorders do not occur in hypernephroma.

To explain the abnormal growth, we need not go beyond my own view that the adrenal secretion underlying general oxidation, metabolism and nutrition, excessive functional activity of the adrenals engenders excessive nutrition and overgrowth. But how account for the malignancy of this form of growth? To answer this would bring us within the domain of pure

[228] Richards: Guy's Hospital Reports, vol. lix, pp. 207-332.

speculation. It is preferable to limit ourselves to clinical facts, pending future developments.

Infants and young children are also subject to a form of primary malignant tumor of the adrenals, described by Hutchison, in which, even before the neoplasm, which grows with great rapidity, can be felt in the renal region, there appears a spontaneous—sometimes traumatic—ecchymosis of one or both eyelids, soon followed by (usually unilateral) exophthalmos and metastasis in the skull, and often in other bones, especially the ribs. The preauricular lymph-nodes and those behind the angle of the jaw are enlarged, and the whole temporal region eventually becomes the seat of a malignant growth. Pain in this location and optic neuritis with amblyopia may complicate the case. Death occurs early from anæmia and cachexia. Of the 14 examples reported, 13 were due to sarcoma or lymphosarcoma of the adrenals.

Diagnosis.—Tumor of the orbit in infants and young children should, as emphasized by Tileston and Wolbach,[229] arouse the suspicion of metastases from an adrenal growth. If an abdominal tumor be found it is almost certainly of adrenal origin, and this would be still further corroborated by enlargement of the preauricular glands, which renders the diagnosis of sarcoma of the orbit unlikely. Chloroma presents almost identical growths, being associated with tumors of the orbit in two-thirds of the cases, with exophthalmos usually as the first symptom, but this may be excluded in the absence of leukæmic changes in the blood. Myeloma may cause bony growths about the skull, but is exceedingly rare in childhood; the presence of the Bence-Jones body in the urine would render the diagnosis of myeloma certain, while its absence is not conclusive. Abdominal tumor associated with precocious maturity is practically certain to be of adrenal origin, if tumors of the ovaries or a retained testis can be excluded. Garrow and Kennan[229a] observed a case in which there was a solitary metastasis in the spinal cord.

Hypernephroma of the Kidney.—It is to renal growths developed from the so-called "adrenal rests" in the kidney, that Grawitz, in 1883, gave the name "hypernephroma." They occur more frequently in the kidneys than elsewhere in the body, and

[229] Tileston and Wolbach: Amer. Jour. Med. Sci., June, 1908.
[229a] Garrow and Kennan: Med. Record, Jan. 17, 1912.

constitute a large proportion of all renal tumors, *i.e.*, 17 per cent.

Hæmaturia is often the first and the most frequently observed symptom of renal hypernephroma, having been noted in 90 per cent. of all cases. The hæmorrhages are usually severe and occur intermittently, weeks and even months elapsing between them. Worm-like clots—thus shaped during their passage through the ureters—are often passed. During the intervals the urine is either clear or it may contain red corpuscles. The hæmaturia is increased by exercise and by manipulation of the region overlying the growths if the latter is sufficiently large to be felt. It may be the only symptom of the growth or precede the detection of the latter by palpation as much as ten years. As a rule, however, the tumor (which occurs in 80 per cent. of all cases) is sufficiently large to be detected much earlier, and sometimes immediately after an attack of hæmaturia. It is located in the loin, often on the right side and two or three finger-breadths below the costal margin. It is at first small—about half the size of a walnut—and is movable in about one-half of the cases. As a rule, palpation causes no pain at first, though it may prove tender when directly pressed upon.

Dull pain in the lumbar region suggesting lumbago may be the initial symptom. This pain gradually increases and, after being centered in the region of the growth, with a sensation of weight, increasingly radiates in various directions, the back, the abdomen, and the testicles. It may come on suddenly and last three or four hours, then be followed by hæmaturia and frequent urination followed by a period of rest during which the urine is slightly albuminous. The urine sometimes contains a few casts, oxalate of lime, and a few corpuscles. During this period of rest a certain stiffness may be experienced on the side of the tumor. Varicocele is frequently observed in these cases, on the same side as the focus of pain; it may develop simultaneous with the latter and disappear when the patient assumes the recumbent position.

While periodical hæmaturia, a tumor and pain in the locations mentioned are typical signs of renal hypernephroma, other phenomena may appear gradually as the morbid process advances. Most important among these are the metastases, which occa-

sionally occur as first signs of the disease. This is especially the case in bone metastasis, which may appear in the vertebræ, the ribs and other long bones, the skull, scapula, etc., *i.e.*, practically any portion of the skeleton. Metastasis may also occur in various viscera, particularly the lungs, the consolidation in the latter suggesting the corresponding stage of phthisis.

The arteries may be thickened and show clearly defined signs of arteriosclerosis, quite in contrast sometimes with the relative youth of the patient, and the blood-pressure be quite high. The skin is not bronzed in these cases, but yellowish and, sometimes, swarthy or smoky, this being replaced by pallor when the end is near. The temperature may be raised, but this rarely exceeds 1° or 2° F.

An important feature in this connection is that bronzing is a characteristic of *insufficiency* of the adrenals, as in Addison's disease, whether due to degeneration, tuberculosis or malignant tumor of these organs or of their nerve supply. In hypernephroma, on the contrary, we have an addition of adrenal substance to the circulation through the secretory activity of the adrenal rests, as shown by the familiar results of adrenal overactivity enumerated—high blood-pressure and arteriosclerosis. The icterus or swarthiness here is due, from my viewpoint, to the continuously high blood-pressure which causes the cutaneous capillaries to become hyperæmic and to expose an increased quantity of the adrenal principle—the component of melanin (we have seen in the early portion of this chapter that melanin is the adrenal principle) to oxidation. The stage of bronzing is not reached, because the pigment is not deposited in the cutaneous tissues, as it is in Addison's disease, but merely supplied to them in excess.

The duration of the disease varies from fifteen weeks to eight years. The patient gradually loses flesh and grows weaker, all the symptoms become aggravated, hæmaturia becoming prominent and causing marked secondary anæmia; moderate œdema of the lower limbs may appear mainly as a result of pressure on some large venous trunk, and delirium sometimes precedes the terminal coma.

Diagnosis.—The pain in the region of the affected kidney, the hæmaturia accompanied by frequent urination, and the local-

ized tumor are the chief diagnostic points among those previously enumerated, but other features may serve to facilitate the diagnosis. Gellé pointed out that fragments of the tumor, which is very friable and often dissociated during hæmorrhages, could be found in the clots passed with the urine. The cells preserve their characters and staining properties. As to diagnosis of the tumor itself after removal, Croftan found (1) that a watery extract of fresh hypernephroma, in keeping with adrenalin and adrenal extracts, provoked glycosuria when injected in the rabbit; (2) that a pure starch solution to which the watery extract of hypernephroma was added contained an appreciable quantity of dextrose, and (3) that the watery extract also possesses the power to decolorize an iodine starch solution. These simple tests make it possible to differentiate hypernephromata from other tumors of the kidney. This is important, since the post-operative prognosis of hypernephroma is much more favorable than that of any other malignant tumor of the kidney. A high blood-pressure tends greatly to insure the diagnosis.

Various disorders may be simulated by hypernephroma, prominent among which is urinary calculus. In this connection the pain is coincident with the hæmorrhage, while in hypernephroma the pain continues after the latter, though greatly relieved. The vermicular and cylindrical shape of the clots in hypernephroma is also suggestive. Cystoscopic examination at this time often reveals these clots projecting from the ureter of the diseased kidney, whose tumor can also, in some instances, be discerned under X-ray examination. Pregnancy is sometimes suggested when the growth projects anteriorly, especially in view of the fact that amenorrhœa sometimes precedes the abdominal enlargement.

Hypernephroma may be mistaken for enlarged spleen. The latter is usually nearer the surface and its mobility on inspiration more marked. It is located on the left side, whereas hypernephroma, in most instances, occurs on the right side. Catheterization of the ureters may serve to indicate, between the periods of hæmaturia, which of the two kidneys is most impaired functionally. The blood count affords little if any information, any diminution of red corpuscles—sometimes to an extreme degree—being readily accounted for by hæmaturia.

Moderate leucocytosis occurs in some cases, but not with sufficient frequency to give this sign any diagnostic importance.

In some cases the symptoms and physical signs other than hæmaturia afford but little help to establish the identity of the tumor, either anteriorly or posteriorly. In that case, the absence of pregnancy being clearly established, an exploratory incision followed immediately, if hypernephroma be present, by its radical removal, is indicated.

Pathology.—Hypernephroma is usually located in the upper pole of the kidney, immediately, therefore, under the adrenals. When found early in life at autopsies it may be no larger than a lentil or even smaller, but it may attain the size of a child's head, growing outwardly or, in some cases, inwardly at the expense of the renal tissues. These growths reproduce more or less perfectly the adrenal tissue, the smaller growths being made up, as a rule, of the cortex, and the larger of both the cortical and the medullary substance. They are firm when small, but when they attain a certain size their tendency is to become lobulated, the projecting masses becoming softer and cyst-like. They are lobulated owing to the fibrous bands derived from the renal capsule, and the lobules when opened may be yellowish, grayish red, or brown or blackish, and contain hæmorrhagic areas—the source of the blood which causes hæmaturia.

The larger growths are those which tend to become malignant and to produce metastases. These occur through the blood-vessels, both the arteries and veins; the bones and lungs, as previously stated, are the structures most frequently invaded, though, occasionally, extension occurs by the lymphatics, including the retroperitoneal glands.

Microscopically, they usually show a scanty stroma composed of vascularized connective tissue in columns and a parenchyma formed of endothelial polygonal or columnar, translucent nucleated cells which differ entirely from those of the renal epithelium. The cytoplasm is granular and contains, besides detritus and giant-cells, numerous fat-laden vacuoles. It is the presence of considerable fat thus disposed which first caused these tumors to be regarded as lipomata. The fat contains lecithin. Glycogen is also present; sometimes in relatively large quantities.

Prognosis.—As a rule, hypernephromata grow slowly at first, months and even years elapsing before they metastasize or show other signs of malignancy. They may then progress very rapidly and, the hæmaturia becoming continuous, death occurs from exhaustion.

When the growth is thoroughly removed before this stage of malignancy is reached, it shows no tendency to recur.

Treatment.—An exploratory incision is warranted, as previously stated, when an abnormal growth in the abdomen or in the region of the kidney occurs coincidently with hæmorrhage, even when other symptoms of hypernephroma are not present. The majority of authorities consider this procedure advisable, even when hæmorrhage into the bladder cannot be accounted for. In some cases discomfort or tension over one kidney, and deep comparative palpation on both sides may suggest which side should be explored first, but if this unilateral examination fails to indicate the presence of a growth exploration of the other kidney is justifiable. In some instances, the organ is merely enlarged, especially toward the upper pole, or at the hilum. Removal of the growth may be performed extraperitoneally through a lumbar incision. The fatty capsule should, according to Kuzmik, be removed along with the growth, as it may be infiltrated and thus lead to recurrence.

CANCER OF THE ADRENALS.

Primary malignant tumors of the adrenals are generally regarded as rare, but it is probable that when the symptomatology of these growths will be known by the profession at large instead of, as at present, by very few of its members many deaths now attributed to Addison's disease in adults and to asthenic disorders in children will be found to be due to this class of growths. Addison, in fact, included these neoplasms among the etiological factors of the disease which bears his name, but it is now plain that the two syndromes differ in many respects, and that the treatments indicated—medical in the one, and surgical in the other—impose the need of recognizing malignant neoplasms of the adrenals as distinct morbid entities.

Varieties.—Primary malignant tumors of the adrenals are of the various forms of *sarcoma* those most frequently met with

and which occur, in the majority of instances, in infancy, childhood, and adolescence; *carcinoma* which occurs, as a rule, in adults or aged subjects. Among the rarer varieties may be mentioned the *malignant hypernephroma* and a class of tumors termed by Prudden *hæmorrhagic adenoma,* i.e., the growths reviewed under the preceding heading. They appear much earlier in females than in males.

While 24 cases of malignant growths collected by Rolleston and Marks included 15 of sarcoma and 9 of carcinoma, 67 collected by Ramsay included 30 of sarcoma and 37 of carcinoma. This tends to suggest that the two forms occur about evenly.

Symptoms.—As a rule, the general phenomena develop insidiously, the adrenal lesion being well advanced when they begin to appear. The strength wanes more or less rapidly; the weight gradually decreases; the pulse and cardiac action become increasingly weaker and more rapid; the temperature shows exacerbation of a couple of degrees at times, but the advanced cases are usually subnormal; the appetite decreases; digestive disturbances, such as nausea, vomiting, flatulence, and diarrhœa, are commonly observed. Anæmia is sometimes manifest, the hæmoglobin being often reduced to 50 per cent., and the red corpuscles to 3,000,000 or less. Cough, with bronchial râles, localized dullness, and hæmoptysis, are occasional complications, while dyspnœa and increase of the number of respirations are apt to occur in advanced cases. The skin may remain normal, but various degrees of pigmentation, ranging from slight icterus to actual bronzing, are observed in the majority of cases. The typical facies may alone be present in cases of primary carcinoma.

This symptomatology is based on an analysis of 60 reported cases of primary malignant tumors of the adrenals. The phenomena are clearly explained by the functions I attribute to the adrenals. Being the purveyors of the secretion which—as the albuminous constituent of hæmoglobin—sustains oxygenation and metabolism and therefore nutrition, increasing emaciation, weakness, hypothermia, the decrease of hæmoglobin, etc., are but normal results, all the other phenoma being secondary thereto. The cases in which no pigmentation of the skin occurs are usually those in which but one adrenal is involved.

All these phenomena are seldom witnessed in a single case. As a rule, after a period of progressive emaciation and adynamia, a tumor can be detected by palpation posteriorly below the costal margin, close to the vertebral column. The mass at first follows the respiratory movements and recedes under pressure, but it eventually becomes fixed and immovable. In some cases, especially in infants, the tumor cannot be detected in this manner, but the abdomen gradually enlarges with a steady increase of the line of dullness, though perhaps no other symptom be discernible. When the outline of the growth can be clearly followed with the fingers, its border is not nodular as in hepatic cancer, but smooth.

Pain is sometimes complained of; it may be located in the region of the tumor; or, radiating upward or across the back, it may extend to the shoulders. The pain has been attributed to the phrenic nerve, but a clearer explanation is the effect of the traction by the tumor, upon the sympathetic ganglia and through the greater splanchnic, upon the sympathetic chain, which is merged in with the mass of nerves, including the brachial plexus, in the tissues of the shoulders.

Pressure symptoms are apt to complicate a case of long duration. Ascites, general œdema, or œdema of the ankles or legs are commonly observed in such cases, due notably in most instances to pressure upon the inferior vena cava. Gangrene of the feet has also been observed. In carcinoma, metastasis is most common in the liver and lungs; in sarcoma it is not quite as frequent and occurs in most cases in the liver and kidney.

Death may occur suddenly, preceded by very few of the above symptoms, especially the sarcomata of infants. In the majority, however, especially in adults, the morbid symptoms gradually develop and the asthenia increases until unconsciousness, labored breathing, and coma terminate in death.

Infants may also suffer from a congenital type of adrenal tumor which simultaneously invades the liver. It is encountered as a congenital tumor, during the first weeks of life. The abdomen becomes increasingly distended; there is moderate emaciation, but no jaundice, pigmentation, ascites, or even pain, the child nursing almost up to the time of death. William Pepper[230]

[230] Pepper: Amer. Jour. Med. Sci., Mar., 1901.

described a series of 6 cases, including a personal case, showing that congenital sarcoma of the adrenals and liver constitutes a special type of malignant disease with its own peculiar symptoms and pathological findings: Swelling of the abdomen occurred within a period ranging from birth to five weeks, thus indicating the congenital nature. The infants lived from one to sixteen weeks, thus showing great malignancy. The increase of growth could be discerned from day to day, thus illustrating rapid development. All were females. The entire normal liver structure was practically destroyed in all. The suprarenal growth exhibited the peculiarity of being very hæmorrhagic. No other part of the body was involved by the new growth.

Diagnosis.—The diagnosis of malignant tumor is not difficult when the tumor is sufficiently large to be discovered by palpation, especially when paræsthesia over the kidneys. This and the asthenic phenomena point clearly to the adrenals, especially if jaundice or any pigmentation of the skin be present. Unfortunately the morbid process is far advanced as a rule when these signs appear. The tumor has been mistaken for psoitis and abscess and phrenic abscess. From hepatic cancer it differs in that the surface of the tumor is smooth instead of lobulated. Of course the possibility of metastasis in the liver, its most frequent seat, must be borne in mind. Hydatid cyst may be suggested, but the absence of the hydatid thrill and other typical symptoms will avoid error. A projecting and enlarged gall-bladder is sometimes simulated by an adrenal tumor capable of displacing the intestines anteriorly; but the latter are much less tense than such a gall-bladder. Abdominal aneurism may be suggested, but the absence of aneurismal bruit and the absence of all other signs of adrenal growth eliminate this source of error. In renal cancer or renal hypernephroma, hæmaturia and other evidences of renal disorder are usually present, while they are more likely to be absent in malignant growths of the adrenals. Pain occurs earlier than in renal tumors, while febrile disturbance is rare in the latter.

Two symptoms, according to Israel,[231] point to involvement of the suprarenal gland: (*a*) Paroxysms of pain and paræsthesias in the absence of a palpable tumor, and (*b*) a febrile course.

[231] Israel: Deut. med. Woch., No. 44, 1905.

The painful paroxysms in renal as well as suprarenal tumors are due to the extension of the neoplasm to the roots of the lumbar plexus. In suprarenal tumors this may occur quite early owing to the immediate vicinity of these structures. On the other hand, in renal tumors the invasion of the capsule usually takes place at a late period when the growth has reached so considerable a size as to become palpable. The fact that fever occurs in cases of suprarenal tumors has hitherto been unknown. Israel observed it in 57 per cent. of his cases, while in renal tumors it was present only in 1 to 2 per cent.

Another apparently characteristic fact in differentiating from renal tumor is that the adrenal growth tends to approach more nearly the median line (in the region from the seventh to the ninth costal cartilages), while the primary tumor of the kidney appears first in the region from the ninth to the eleventh. Tumor of the adrenal at the time of its presentation beneath the margin of the ribs appears broader than does that of tumor of the kidney, and the lower contour of the tumor of the adrenal is much less rounded than is that of the kidney.

The emphasis laid by Israel on the presence of fever in adrenal malignant neoplasms affords striking proof of the correctness of my contention, urged ever since 1903, that the adrenals, through the rôle of their secretion in oxidation and metabolism, were the active organs in fever—a process which pathologists have failed to explain.

Leucocythemia is sometimes simulated; but the absence of myelocytes and other characteristics soon eliminate this disease.

Ecchymosis of the orbit of unaccountable origin in infants and young children or tumor of the orbit should cause careful search for manifestations of malignant tumors of the adrenals, as previously stated.

Treatment.—Removal is the only resource, but as a rule the result is unsatisfactory owing to the fact that the presence of the growth is recognized only through metastasis; or when it has developed to a marked extent, and produced either through metastasis, pressure, etc., disorders in other parts of the organism which cannot be reached.

Cases in which the tumor involves one adrenal only, as suggested by the absence of symptoms of adrenal insufficiency,

marked asthenia, emaciation, hypothermia, etc., and the presence of a tumor and hyperæsthesia on one side only, offer a better chance of success, since they indicate that the other adrenal will probably be able to subserve alone the needs of the organism. The chief difficulty encountered in the course of the operation is a marked tendency to hæmorrhage owing to the friability of the morbid tissues.

CHAPTER III.

THE THYROPARATHYROID APPARATUS IN GENERAL OXIDATION AND IMMUNITY.

We can no longer speak of the thyroid gland as a functional entity. The two external parathyroid glandules, discovered in 1880 by a Swedish physician, Sandström, and the two internal parathyroid glandules, discovered by Nicolas,[1] of Nancy, in 1893, and independently by Kohn,[2] of Prague, in 1895, introduced a new era in our conception of this organ. Foreign investigators, therefore, tend increasingly to adopt the term "thyroparathyroid apparatus" owing mainly to the anatomical relationship between the glandules and the thyroid vessels, with which their own circulation is directly connected. We shall see, however, that many physiological facts, the first of which were pointed out by Gley, of Paris, in 1892, and clinical observations warrant the use of this compound term.

PREVAILING VIEWS AS TO THE FUNCTIONS OF THE THYROID AND PARATHYROIDS.

In 1859, Shiff, of Geneva, found experimentally that removal of the thyroid gland in the dog caused violent nervous disorders and death. Two surgeons of the same city, the brothers J. L. and A. Reverdin, then pointed out (1882) that in certain goitrous subjects, and after the complete removal of goiter in otherwise normal subjects, there also appeared marked trophic and nervous disturbances. This was confirmed the following year by another Swiss surgeon, Kocher. The principal postoperative phenomena noted were: marked weakness and fatigue, a sensation of cold, pallor, muscular stiffness, and pains; œdematous thickening and pallor, hardness and dryness of the skin, the normal folds being more or less effaced, and loss of hair. The main nervous and mental phenomena were: tetany, sometimes attaining the violence of true tetanus and passing into

[1] Nicolas: Bull. de la Soc. des Sci. de Nancy, vol. v, p. 13, May 3, 1893.
[2] Kohn: Archiv f. mikrosk. Anat., Bd. xliv, S. 366, 1895.