THE GOULSTONIAN LECTURES

ON

THE SUPRARENAL BODIES.

Delivered before the Royal College of Physicians of London,

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LECTURE I.

THE ANATOMY, HISTOLOGY, AND MORBID ANATOMY OF THE SUPRARENAL CAPSULES.

[In his preliminary remarks the lecturer thanked the College for the honour conferred on him, and said that since the suprarenal capsules were attracting considerable attention at the present time, it seemed opportune to review the state of our knowledge concerning them.]

Method of Removal.—The most satisfactory method of examining the suprarenal bodies and removing them in the course of a necropsy was described.

THE RIGHT SUPRARENAL CAPSULE.

The right suprarenal capsule embraces the inner, upper, and anterior part of the corresponding kidney. Its outline, as seen from the front, is roughly triangular, with angles pointing respectively (1) outwards, (2) upwards, and (3) downwards. It is flattened and presents two surfaces, anterior and posterior, each of which is divisible into two secondary areas.

The anterior surface is not uniformly flat; along its upper and inner borders there is a continuous depressed area. This bears a varying proportion, one-third to a-half, to the whole extent of the anterior surface, usually about a third. The two areas thus formed on the anterior surface are separated by a furrow. The furrow is overhung by the margin of the larger, outer, and comparatively elevated area.

Section of the suprarenal capsule shows that the furrow corresponds to a projection on the posterior surface.

This undulation on the anterior surface follows the curve of the upper and inner borders. At a point on this undulation, corresponding to the upper and inner angle, the suprarenal vein issues from the medulla in the furrow, and runs upwards to enter the inferior vena cava.

The depressed area is uncovered by peritoneum; the part which lies adjacent to the upper border is in immediate contact with the right lobe of the liver, while that part which corresponds to the inner border lies underneath the inferior vena cava.

The remaining or elevated area on the anterior surface presents (1) a non-peritoneal portion (Anderson)¹ for the hepatic flexure of the duodenum near its lower angle; the extent of this portion varies very considerably (St. John Brooks);² and (2) a portion covered by the peritoneum forming the hepato-renal fold.

The posterior surface is divided by a projection into two secondary areas. This projection, which is the counterpart of the furrow on the anterior surface, fits into the groove between the kidney and the right crus of the diaphragm. This undulation in the suprarenal body is oblique, and the process on the posterior surface looks outwards. Of the two secondary areas the inner is flattened by the pressure of the right crus of the diaphragm, and is larger than the outer area, which is so tilted upwards by the underlying kidney that it looks backwards and downwards.

THE LEFT SUPRARENAL CAPSULE.

The left suprarenal capsule is applied to the inner margin of the upper half of the left kidney, which it overlaps; it passes into the upper margin of the kidney for a short distance only. The inner border is convex, and looks slightly upwards; the outer border is concave. There are two angles: the upper which is pointed, and the inferior rounded and covering the renal vessels. There are two surfaces— anterior and posterior. The anterior has a crescentic outline. It is flat, and traversed by a groove or furrow, from which the suprarenal vein runs downwards to join the left renal vein.

This groove runs from above downwards and inwards, and thus divides the anterior surface into two secondary areas: (a) an outer and inferior, and (b) an inner and upper. Near the superior angle these areas are of equal size, but below the outer becomes the larger, and forms the lower rounded angle of the suprarenal body.

Relations of the Anterior Surface.—The anterior surface is divided into (1) an upper portion covered by the peritoneum of the lower sac, and in relation with the cardiac end of the stomach near the entrance of the œsophagus, and below that with the superior extremity of the spleen; and (2) the lower part uncovered by peritoneum, and in direct contact with the pancreas and splenic artery. On the posterior surface there is a projection corresponding to the furrow on the anterior surface. This projection passes between the kidney and the crus of the diaphragm almost at right angles to the plane of the anterior surface. This undulation is vertical, thus contrasting with the oblique undulation in the right suprarenal body. External to the projection there is the external area larger than the internal. This external area is thin, and is expanded by the pressure of the underlying kidney. The renal vessels as they pass into the hilum lie under cover of this area. Internal to the projection is the smaller internal area which rests on the crus of the diaphragm; it is thick and compact, and may cover the left semilunar ganglion, but this is not a constant relation.

ANATOMICAL CONFORMATION.

The different folding, as shown by the oblique and vertical directions of the undulations respectively in the right and left suprarenal bodies, depends on the differences in the packing of the two organs. The probable explanation of the more complicated form of the undulation on the right side is the close relation to the firm liver, and the pressure thereby exerted on the suprarenal body. Each of the organs weighs about a drachm or rather more, the left being rather the heavier.

In cases where the kidney is displaced, the corresponding suprarenal capsule remains in its normal position. When a horseshoe kidney exists the position of the suprarenal bodies undergoes no change, even though the kidney is situated over the promontory of the sacrum. In an example of this kind the suprarenal bodies lay on the crura of the diaphragm, and were flat and not thrown into their normal undulations. This observation shows the influence which the pressure normally exerted by the kidneys has on the conformation of the adrenals.

The suprarenal body has a firm capsule of fibrous tissue, and running in from it are septa containing small arteries which traverse the cortex and reach the medulla.

The arteries derived from the aorta, renal and phrenic arteries, enter the cortex and pass inwards towards the medulla: at the hilum the cortex thins away and exposes the medulla, from which the suprarenal vein issues.

The suprarenal vein in the medulla is surrounded by large bundles of smooth muscular tissue, which form a prominent feature on section. Guarneri and Magini³ suggest that the circulation through the organ may be slowed by the contraction of these muscular bundles.

In foetal life the large and very vascular suprarenal capsules are relatively, though not absolutely, larger than in adult life. Their large size and vascularity make it probable that their functions are more extensive and active in foetal life. At the third month of intrauterine life the kidneys and suprarenal capsules are of the same size; at the sixth month the kidneys are twice the size of the suprarenal capsules and more than twice their weight. At birth the kidneys are about three times heavier than the suprarenal capsules, while in adult life, the kidneys weighing on an average 5½ ounces and the suprarenal bodies 1 drachm each, the relation is 44 to 1. After birth the suprarenal capsules continue to increase in size, and, like other organs, attain a size varying roughly with that of the whole body. At what time they cease to grow it is impossible to say; but the general impression left on my mind from examining more than 1,000 pairs is that they are larger about 40 years of age than at other periods of life. Probably some of the increase in size is due to fatty change. Their growth after birth shows that they cannot be regarded as mere foetal relics.

In old age they diminish in size and, like other parts of the body, contain less fat.

It is often stated that the suprarenal bodies are larger in negroes than in the white races. Duckworth⁴ mentions five dissections of negroes in which the suprarenal capsules were not larger than in whites. Professor Macalister has kindly informed me that in four negroes and in one Malay dissected by him the suprarenal bodies presented no unusual features.

ABNORMAL SUPRARENAL BODIES.

The different shape of the two suprarenal bodies depends on their different relations and packing. I have seen the left expanded, and the right approaching the shape of the left.

I have met with abnormal projections from the suprarenal body on both sides. The figure, from a photograph kindly done by Mr. W. Paul Jones, shows one on the right side. If more pedunculated it might resemble in appearance an accessory suprarenal body.

Fig. 1.—Right suprarenal body with abnormal process; nearly twice natural size.

In anencephaly and hemicephaly the suprarenal capsules may be atrophied or absent; on the other hand, they may be normal. Alexander⁵ has not been able to find any cases of fetuses in which atrophy of the suprarenal bodies was associated with a normally developed brain and spinal cord.

Zander⁶ attributes the atrophy of the suprarenal bodies to the maldevelopment of the nervous system; while Alexander considers that the primary lesion is in the suprarenal bodies, and that suppression of their function is one, among several, of the causes influencing the development of the central nervous system. This view is of considerable interest in connection with the severe lesions which Tizzoni found in the brain and spinal cord as a result of removal of the suprarenal capsules.

ACCESSORY SUPRARENAL BODIES.

Accessory suprarenal bodies are very commonly present in the connective tissue in the immediate neighbourhood of the two organs. They are found when looked for, but do not otherwise, as a rule, attract attention, as they are so small. They are yellow in colour, oval or round, and usually about the size of a grain of corn. They are often in contact with the main organ, or may be attached to it by tags of fibrous tissue, of various lengths, containing small vessels.

The number of accessory suprarenal bodies varies. I have seen as many as five on one side (the right), but this was in

a case in which that capsule contained caseous material, so their presence may have been the result of some compensatory hypertrophy taking place, especially as the case was that of a boy of 17 years dying of chronic phthisis without any symptoms of Addison's disease. Stilling⁷ has shown that hypertrophy of accessory adrenal bodies may take place in young animals after the experimental removal of the organs. Although there is no evidence of compensatory hypertrophy occurring in adult man, it is possible that it may occur in early life. The largest accessory suprarenal I have seen was as large as a cherrystone, and was attached by a loose tag of connective tissue to the right suprarenal.

The accessory suprarenal bodies may be found among the fibres of the renal or solar plexus and in close relation to the semilunar ganglia. It is said that accessory suprarenal bodies may occur in the substance of the main organ, but it is probable that the structures observed were adenomata or portions of a much convoluted suprarenal body cut in section. The presence of accessory suprarenal bodies in such distant parts as the broad ligament of the uterus and along the course of the spermatic vessels was pointed out by Marchand,⁸ and explained on embryological grounds. Examples of accessory adrenal bodies on the spermatic vessels near the inguinal canal are quoted by Schmorl.⁹

Structurally the larger accessory suprarenal bodies show a division into cortex and medulla, while in the smaller ones this is not the case.¹⁰ In children the cells are not pigmented, while in adults pigment is present.

SUPRARENAL "RESTS."

Instead of being in the loose connective tissue, accessory suprarenal bodies may be found embedded in the kidney or liver, and are then often spoken of as suprarenal "rests." They are more commonly recognised in the kidney than in the liver, though Schmorl records four examples of suprarenal "rests" occurring in the liver in 510 examinations. In these four cases the "rests" were in the right lobe of the liver. This writer thinks it probable that the liver tissue surrounds the accessory suprarenal bodies, as in two of his four cases the right kidney was displaced, and the resistance to the growth of the right lobe of the liver, normally due to the adjacent kidney, was absent.

In the kidney suprarenal rests appear in two forms: (1) The commoner, small round masses embedded in the cortex, and often so extensively degenerated into fat, that they have been called "renal lipomata."¹¹ They resemble the dried-up cysts not uncommonly seen on the cortex of the kidney. Like the suprarenal rests in the liver they may be multiple. They occur in any part of the cortex of the kidney. Histologically they have been described as conforming in different cases to the type of each of the three zones in the cortex of the suprarenal capsule, or even to the medulla. (2) Flattened plaques of suprarenal tissue, the medulla being represented as well as the cortex, which are placed partly inside, partly outside, the capsule of the kidney. Dr. Newton Pitt¹² has described this condition on both sides; I have seen it on one side. This condition occurs in the upper part of the kidneys, where pressure is exerted by the liver and spleen. The pressure probably flattened out the accessory suprarenal bodies or rests, so that the difference in form of these two varieties is due to their respective positions.

THE HISTOLOGY OF THE SUPRARENALS.

The Cortex.—The cortex is usually described as consisting of an outer zone (the zona glomerulosa), lying internal to which are the zona fasciculata and the zona reticularis; between the latter and the medulla no hard and fast line can be drawn. The cells found in the cortex are large epithelial cells, which have been compared by Creighton¹³ to the cells in the stratum granulosum of a Graafian follicle. The cells in the outer part of the cortex are larger than those in the inner, the transition being a gradual one. The arrangement of the cells, especially in the zona glomerulosa, has suggested the idea that there are capillary ducts between the cells, but nothing very definite can be made out. The radial arrangement of the cells in the cortex probably depends on the septa, blood vessels, and lymphatics running inwards towards the medulla.

The cells of the cortex very readily become occupied with

large globules of fat; this is so commonly met with in adults as to be considered normal. The presence of extensive fatty change and the much smaller relative size of the suprarenal capsules to the rest of the body in adult life make it probable that the function or functions discharged by them are more active in foetal life.

HISTOLOGY.

Ganglion cells are described as being sometimes seen on the outside of the cortex, but are never present in the substance of the cortex. In the inner part of the cortex small vascular dilatations may be seen between the cells.¹⁴

The cells in the innermost layers of the zona reticularis are granular, and stain brown with chromic salts; they resemble the cells of the medulla, and contain a varying amount of pigment. The presence of granules in the cells is of interest, as they are possibly the precursors of a material secreted by the cells—a zymogen, analogous to that of secretory glands. In negroes the cells of the cortex are said to be extensively pigmented.

Canalis¹⁵ has observed indirect nuclear division in the cortex of adult animals, and concludes from this that the suprarenal bodies remain functionally active. By the kindness of Dr. Hill, Master of Downing College, Cambridge, I am allowed to mention his, as yet unpublished, opinion that from active mitosis occurring in the deeper layers of the zona reticularis, it appears probable that the growth of the adult suprarenal capsule occurs in that situation, and that the cells pass outwards to form the cortex, and inwards to form the medulla. Gottschau¹⁶, however, believes that the cell formation goes on in the zona glomerulosa and outer part of the zona fasciculata, and that the destruction of cells which takes place in the zona reticularis and medulla provides some substance of unknown function, which passes into the blood.

The extreme frequency with which a fatty condition of the outer part of the cortex is met with, makes it somewhat improbable that these cells are responsible for the growth of the organ. These facts, together with the absence of karyokinesis from the medulla,¹⁷ make it highly probable that the suprarenal body grows from the zona reticularis.

THE MEDULLA.

The cells of the medulla are of different forms; some of them appear to be branched, but their outlines are far from easy to make out. A rodlike appearance of the cells, like that seen in the convoluted tubes of the kidney, has been described by Guarnieri and Magini.¹⁸ The cells of the medulla are granular.

When fresh the cells of the medulla stain brown with bichromate of potassium. This reaction is only obtained soon after death; it becomes less marked as the interval increases, until, twelve hours after death, it is completely lost. Stilling¹⁹ describes these cells as chromophile, and in animals he finds them in the sympathetic and intercarotid gland as well as in the suprarenal body. These cells stain blue with persulphate of iron.

The brown reaction with chromic salts of the cells of the medulla has long been known; it appears to have been first pointed out by Henle. Creighton²⁰ says that this coloration affects the nuclei and also the blood in the lacunar spaces between the cells of the medulla, while recently Manasse²¹ has noticed in suprarenal bodies hardened in Müller's fluid homogeneous, brown material in the veins, which he traced to its origin in the cells of the medulla. These appearances could not be made out in specimens hardened in spirit, as spirit dissolves this "hyaline" material. Auld²² regards the medulla as a tubulo-alveolar gland, and describes colloid matter as being present in its acini at rare intervals. If these acini are in reality blood spaces, the colloid material described by him, and the hyaline casts of Manasse, would appear to correspond to each other.

Guarnieri and Magini describe cylindrical bodies with a refractive index between, or more often inside, the cells of the medulla, which do not appear to be fat, and which may be the same as the bodies described by Auld and Manasse.

The cells of the medulla do not become so readily infiltrated with fat as those of the cortex, but they certainly do to a minor degree, though Alexander considers that very possibly the particles are not fat, but something else.

Orth refers to a green coloration of the medulla on adding a solution of perchloride of iron as a sign of chromogen in the cells of the medulla.

Much discussion has taken place as to the existence of ganglion cells in the medulla. These are all transitions between typical epithelial cells and cells which, if met with elsewhere, would be described as ganglion cells. Leydig and Luschka considered the cells of the medulla to be nerve cells. Virchow and most writers describe ganglion cells as being present. Auld describes ganglion cells and modified ganglion cells. Holm²³ has described large cells with large nuclei, which he calls "doubtful ganglion cells"; they are, however, probably the groups of epithelial cells found surrounding grey nerve fibres described by Guarnieri and Magini.²⁴

Alexais and Arnaud,²⁵ and Guarnieri and Magini,²⁶ deny the existence of any nerve cells in the medulla.

Probably there are some few ganglion cells in connection with the numerous grey nerve fibres present in the medulla, which form a network, and have in places groups of epithelial cells surrounding them; in their description of these non-medullated nerve fibres Guarnieri and Magini say they have never been able to find their termination. Fusari,²⁷ using Golgi's silver nitrate method, has found a delicate fibrillar termination of the nerve fibres between the cells.

The medulla contains a reticulum of connective tissue, in which lie epithelial cells and blood sinuses with thin walls, which receive the blood from the arterioles of the cortex, and eventually open into the central vein. The vessels of the suprarenal capsules, with the exception of the central vein, have thin walls composed of little more than endothelium. Lymphatic vessels have been described between the cells. The blood spaces are surrounded by the cells, so that there is some resemblance to the arrangement in the liver of cells and capillaries; Manasse has described groups of cells projecting into the lumen of the veins, and pouring out, as a kind of secretion, brown hyaline matter.

RELATION OF THE CORTEX AND MEDULLA TO EACH OTHER.

At the present time the cortex and the medulla of the suprarenal body are generally considered to be distinct in origin, structure, and function. The cortex is regarded as being glandular or hæmatopoietic, and the medulla as being nervous and connected with the sympathetic.

From an embryological standpoint Balfour and Mitsukuri²⁸ have shown the medulla to be connected with the sympathetic, and the cortex to be derived from the mesoblast. Weldon²⁹ considers the suprarenal cortex to be derived from the Wolffian bodies, and that it secondarily encloses blood vessels and nerves to form the medulla.

In connection with the view³⁰ that the adrenal bodies are derived from the germ epithelium, the observations of Creighton³¹ are interesting. In the cortex of the horse and of the dog he occasionally found tubes resembling the aborted Graafian follicles of the ovary; he therefore divides the suprarenal body into two parts—these tubes in the cortex, and the remainder (which consists of ordinary medulla and most of the cortex). These tubes degenerate and pass into the ordinary cortex—in the horse fading into the zona fasciculata, in the dog into the zona glomerulosa. These tubes correspond to the follicles in the cortex of the ovary, while the remainder corresponds to the stratum granulosum in the corpora lutea and to the interstitial cells of the ovary.

The distinction between the cortex and medulla of ordinary anatomy Creighton considers quite arbitrary, as there is no real difference between their constituent cells. The central part or medulla is only more spongy than the rest. Arnold³² considers the difference between the cortex and medulla as being due to modifications in the arrangements of the interstitial supporting tissue and of the blood vessels, and draws attention to groups of cells near the central vein which closely resemble the zona glomerulosa.

At the sixth month³³ of intrauterine life there is no difference between the cortex and the medulla, if the sympathetic nodules which are about to disappear be excluded, and on the microscopic examination of the adult organ the transition is seen to be very gradual.

From these considerations I should be inclined to regard the suprarenal as a functional whole, the medulla and cortex

performing the same work, though possibly in unequal degrees, since the cortex very commonly undergoes considerable fatty change. This speculation, based on anatomical grounds, receives strong support from the observation that the medulla alone provides an active extract.³⁴

VARIOUS MORBID CONDITIONS OF THE SUPRARENAL BODIES.

ATROPHY.

How often atrophy of the suprarenal capsules occurs does not seem to have been investigated, and its presence is only recorded when there were indications of Addison's disease during life. The suprarenal capsules normally diminish in size in advanced life. In an examination of the organs in 1,050 *post-mortems* I found them small in 6 cases under the age of 45; in 3 both were small, and there were no signs suggesting Addison's disease; in 1 case there was castration in the right and atrophy of the left without any symptoms; and in 2 cases of phthisis, where there was slight pigmentation, the suprarenal bodies were small. I have never seen the extreme degree of atrophy described in some cases of Addison's disease in which the organs were reduced to the size of peas.³⁵

HÆMORRHAGE INTO THE SUPRARENAL CAPSULES.

As the result of severe injuries, such as fracture of the spine or rupture of the liver and spleen, blood is often poured out around the suprarenal bodies. Hæmorrhage into the suprarenal bodies is not infrequently met with under these conditions; the extravasation is almost always into the medulla.

As the result of traumatism during birth hæmorrhages frequently occur into the suprarenal capsules. On an examination of 130 stillborn children Dr. H. Spencer³⁶ found extravasations into these organs in 26; in 2 of these the hæmorrhage occurred in the cortex, in the remaining 24 it was into the medulla, and in half the cases it was bilateral; in 3 cases the hæmorrhage had ruptured the capsule. These hæmorrhages occurred more often in difficult labours, and were more frequently met with in pelvic than in cephalic presentations.

The question as to what changes take place in the suprarenal capsules as a result of such extravasations, if the child lives, is an interesting one. Wainwright³⁷ has recorded the case of a child 2 months old in whom the suprarenal bodies showed changes which were probably due to imperfect absorption and organisation of blood extravasated into the medulla. It is possible that organisation of extravasated blood might finally result in the cirrhotic atrophy of the adrenals, which, when bilateral, has been associated with the symptoms of Addison's disease. Unilateral atrophy with a fibrous increase, which is sometimes met with accidentally, could thus be explained by a former unilateral hæmorrhage.

Apart from traumatism hæmorrhage into the medulla of the suprarenal capsules has been recorded in a variety of conditions, in which the most common factor is venous congestion.

CLOUDY SWELLING.

Softening and cloudy swelling of the suprarenal capsules occur in febrile conditions, and it is noteworthy that the spleen and the adrenal bodies show very similar changes under these conditions. The medulla appears sodden and blood-stained, and microscopically small extravasations may be found in the cortex. The softening often leads to a separation between the cortex and the medulla, and thus produces an apparent cavity. This ancient observation finds a permanent record in the term "capsule."

In pyæmia small vascular streaks in the cortex, or more rarely minute abscesses, due to embolism, may occur. In pyæmia set up experimentally in guinea-pigs, Langlois and Charrin³⁸ have described swelling and hæmorrhages in the suprarenal bodies.

FATTY CHANGE.

Fatty change is so commonly met with in the suprarenal bodies of adults as to be generally considered a normal condition, while in young children these organs have hitherto been thought to be free from fat. The fat occurs as large globules in the cells. This change may be present throughout the whole of the cortex, or be best marked in the zona fasciculata. The medulla is occasionally seen to be

occupied by fat, but never to the same extent as the cortex. Atlee,³⁹ in a paper as yet unpublished, has recorded the results of the examination of the suprarenal bodies in infants.

In marasmic infants the suprarenal bodies were found to be extremely fatty (Fig. 2), and to have undergone this

Fig. 2.—Suprarenal body stained with osmic acid showing extensive fatty change. Marasmic infant. Low power.

change more constantly than the liver. Thus in nine cases the cortex showed fatty change in all, and in six of them the medulla was also affected, while in eight of these cases in which the liver was examined it was found to be affected in four and normal in the other four.

In stillborn children, on the other hand, fatty change was found to be very moderate in degree and slight as compared

Fig. 3.—Cortex of suprarenal body from stillborn child, very little fat. High power.

with that seen in marasmic children, while in children dying

from diseases other than marasmus fatty change was found, but not to the same extent as in that condition. As far as my observations go, they agree with these results. (I am indebted to Dr. Attlee for Figs. 2 and 3).

Experimentally, Attlee found that in young rabbits in which the suprarenal bodies normally are free from fat, starvation gave rise to marked fatty changes in these organs, and that here, as in marasmic infants, the liver might escape. Martignotti⁴⁰ made the curious observation that starving guinea-pigs for three or four days increased the normal amount of karyokinesis in the cortex. In adult rabbits the suprarenal capsule may normally show considerable fatty change, but starving, extensive suppuration, and poisoning, whether acute or chronic, appeared to give rise to marked fatty change. With regard to these changes two questions arise (1) what is the nature of the change, and (2) what is the significance of its occurrence?

The large size of the fatty globules, the distribution of the fat in the cortex, which, since this area receives the blood first from the branches of the suprarenal arteries, may be thought to be analogous to fatty infiltration of the liver, and the frequent association of fatty infiltration in the liver and subcutaneous tissues (obesity) points rather to its being a storage or infiltration of fat. The occurrence after experimental poisoning and in marasmus, on the other hand, would favour the view that it is a degenerative change. Since it is difficult, perhaps unimportant, to decide as to its nature, it is perhaps best to describe it as a fatty change. As to the significance of the change, its presence accords with the recent observation that the cortex does not yield the active principle⁴¹ of the suprarenal extract, and that relatively the suprarenal bodies are far more active in early life than afterwards.

After removal of one suprarenal body in young animals, Stilling⁴² noticed that the remaining one hypertrophied; while so doing fat disappeared from the cortex for a time but returned after some weeks. Fatty change, though it may be a result of morbid processes elsewhere, cannot be said to give rise to any symptoms on its own account. It is interesting to note that while atrophy of these organs may be associated with symptoms of Addison's disease, fatty change has no such causal relation.

LARDACEOUS DISEASE.

When attacked by lardaceous disease the suprarenal capsules appear but slightly increased in size, and have a somewhat translucent appearance on section. On applying the iodine test the cortex becomes a dark brown, while the medulla remains of a grey or greyish yellow. The appearance thus presented is the reverse of that seen in health. The suprarenal bodies are among the organs which undergo the lardaceous change comparatively frequently. In fifteen cases of well-marked lardaceous disease I found the suprarenal capsules affected in eight; in three of the cases it was slight, so that microscopic examination was necessary to determine its presence.

According to Cornil and Ranvier⁴³ it is rare, and only attacks the vessels of the medulla. In my cases, however, it was always best marked in the vessels running vertically through the cortex; and, though it may be present in the medulla, it is always less marked there than in the cortex. Orth⁴⁴ describes the lardaceous change as occurring chiefly in the region of the zona fasciculata.

CYSTS.

Cysts in the suprarenal body are very rare; the occurrence of echinococcus may be mentioned,⁴⁵ and cysts the result of former hæmorrhages have been met with. I have seen a cyst the size of a cherry containing tenacious fluid. Virchow has suggested that cysts may be formed by a softening down of adenomata of the suprarenal capsules. In primary sarcomata of the suprarenal bodies cysts frequently occur.

TUBERCLE.

In general tuberculosis a few scattered miliary tubercles are occasionally seen in the cortex. In chronic tuberculosis the inflammatory process begins in the medulla. In the early stages, before caseation has occurred, the inflammatory granulation tissue has a firm speckled appearance, and

microscopically contains numerous vessels. Caseation, softening, or calcareous infiltration, may all follow as in other tuberculous formations, but it is highly improbable that caseous material is ever absorbed or disappears. Tubercle is frequently found without any signs or symptoms having been present. In 1,050 *post-mortems* in which I have examined the condition of the suprarenal bodies, there were 131 cases in which death was directly or chiefly due to tuberculous disease, and in 18 of these cases there was caseation in the suprarenal capsules, without there being any evidence of Addison's disease. In 11 instances the caseation was unilateral, and in 7 bilateral.

In the decennial periods it is noteworthy that in the 23 cases in which death occurred under 10 years of age, no tubercle was found in the suprarenal bodies, while out of 17 cases in the period between 10 and 20 years of age caseation occurred twice on both sides and three times unilaterally.

There appears, therefore, to be immunity from tuberculous inflammation in the first few years of life in the case of the suprarenal bodies:

Years.....	1-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	Total.
Cases of tubercle...	23	17	29	29	17	10	5	1	131
No. of tuberculous suprarenals	0	5	2	6	1	2	2	0	18

SYPHILIS.

Gummata are occasionally found in the suprarenal bodies.

ACTINOMYCOSIS.

Extension of an actinomycotic abscess from the right lobe of the liver into the right adrenal body has been recorded.⁴⁶

SIMPLE TUMOURS.

Adenomata may be of two kinds, of which the first is much the commonest: (1) Multiple small yellowish nodules, situated on the cortex of the organ; they are not marked off by any capsule from the surrounding tissue, but differ from it in being the seat of very advanced fatty change. In other respects, the cells composing them are like the cells of the suprarenal cortex. They are sometimes mistaken for tubercles undergoing caseation; in this connection it is well to remember that chronic tuberculosis begins in the medulla. Virchow described adenomata of the medulla as gliomata, taking the view that the interstitial tissue of the medulla was akin to neuroglia. Manasse⁴⁷ has described giant cells in adenomata; I have never met with this appearance. (2) Large adenomata are almost always found singly in the suprarenal capsule, though they may be bilateral. They do not involve the whole of the organ, but form distinctly localised tumours, which may attain a very considerable size. They arise as a rule in the cortex, either from one or from more of its zones, and project usually from one side, though the whole thickness of the organ may be affected. They are a magnified edition of the small multiple suprarenal adenomata. Small ones may be present with them in same organ.

The cells contain a large amount of fat, and this accounts for the pale yellow colour of the adenomata. They may be distinguished from sarcomata by the absence of extravasation into their substance, and by their microscopic structure. Occasionally the fatty change is so advanced that they appear softened or necrosed. Commonly they have no more supporting fibrous tissue than the rest of the organ, but in other cases the quantity of fibrous tissue is much in excess, so that the term fibro-adenoma may be used. I have seen an example of this variety in which the cells did not show any fatty change, and in which hyaline degeneration of the vessels, which were numerous, was well marked.

Virchow described them under the name of struma lipomatosa suprarenalis; and recently from analogy they have been termed adrenal goitres, though it must be regretted that a name of such purely local application as goitre should be applied to a tumour in the abdomen.

Suprarenal "rests" taking on adenomatous growth in the kidney are, according to Horn,⁴⁸ responsible for some of the tumours which have been called adenoma of the kidney.

The existence of adenomata or hyperplastic tumours of the suprarenal bodies suggests the interesting speculation whether any symptoms can be correlated with this condition. Addison's disease and myxœdema have some analogies. Exophthalmic goitre is apparently due to altered structure and secretion of the thyroid gland. Is there any disease analogous to Graves's disease connected with the adrenals? The absence of any symptoms in association with adenoma or hyperplasia of the suprarenal bodies may be due to the fact that they nearly always show extreme fatty change, and so cannot be functionally active. Schäfer and Oliver⁴⁹ have quite recently shown that the cortex does not yield the active principle of suprarenal extract; hence hyperplasia of the cortex would not lead to any modification of the suprarenal secretion. A specimen of ganglionated neuroma has been described.⁵⁰ Dr. Payne⁵¹ has recorded a case of angioma of the suprarenal capsule; there were similar growths in the ovaries and many in the liver.

PRIMARY MALIGNANT GROWTHS.

Both carcinoma and sarcoma of the suprarenal capsules have been described, but generally the histological structure seems to be a vascular rather large-celled sarcoma. In some cases both organs have been the seat of primary malignant growths. The growth starting in the suprarenal body expands it, and may grow down the suprarenal vein or into the inferior vena cava.

By direct continuity the growth often invades the upper part of the kidney and, on the right side, the corresponding lobe of the liver. In some cases the growth may involve the pelvis of the kidney and give rise to hæmaturia. When the growth is extensive and invades the whole of the kidney, it is necessarily very difficult to say whether it began in the suprarenal or in the kidney. Secondary growths occur in the liver most frequently, but also in the lungs, kidneys, bones,⁵² and skin.

Dr. Dickinson⁵³ mentions that in a case of sarcoma of the suprarenal body, the colon did not form an anterior relation of the tumour, as is the case in renal tumours; and since reading this I have seen two cases in which the tumour appeared above the colon, which was somewhat displaced downwards. The soft vascular growths have a tendency to necrose, and so to become excavated into hæmorrhagic cysts; a specimen of a cystic sarcoma as large as a cricket ball is in the London Hospital Museum.

In young children excessive development of hair and of the genital organs has been noted in connection with suprarenal sarcoma.

H. Morris and Sutton speak of tumours of the suprarenal bodies which give rise to secondary growths as being analogous to those rare and interesting cases of bronchocele⁵⁴, which produce secondary growths in bone and elsewhere. Morris⁵⁵ described the growth in one of these cases as being composed of tissue like that on the medulla of the suprarenal body. It seems difficult to distinguish between such a tumour and a vascular large round-celled sarcoma.

Sutton⁵⁶ described an adenoma of the suprarenal body in a marmot giving rise to numerous secondary nodules on the liver, which on section presented a curious mottled appearance, and also to a single nodule in the spleen. Histologically the growth resembled suprarenal cortex, and was therefore not considered malignant. Abnormally low bodily temperature has been noticed in primary suprarenal sarcoma,⁵⁷ but the temperature in a rapidly growing sarcoma from the right suprarenal body⁵⁸ in a coloured girl aged 8 was on an average 100°.

Examples of renal sarcoma arising in suprarenal "rests" have been described. Not only is their structure much like that of primary suprarenal sarcoma, but they show a similar tendency to the formation of hæmorrhagic cysts and to undergo necrosis. Lubarsch⁵⁹ has found glycogen in eight cases, and regards this as indicating their embryonic origin. Schmorl⁶⁰ suggests that some of the primary neoplasms of the liver may similarly be due to proliferating changes in a suprarenal "rest."

SECONDARY GROWTHS IN THE SUPRARENAL BODIES.

In 1,050 *post-mortem* examinations carcinoma of various parts of the body occurred 63 times, and in 7 of these the suprarenal bodies contained secondary growths.

There were 24 cases of sarcoma, and of these only 2 cases showed metastatic growths in the suprarenal bodies.

Norman Moore,⁶¹ in 123 cases of new growth (102 carcinoma, 21 sarcoma) found secondary growths in the suprarenal bodies in 8. Three of these were carcinoma, 3 sarcoma, and 2 are described as endothelioma, the primary growth being in both cases in the heart.

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THE PATHOLOGY OF OEDEMA.¹

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THE subject of œdema has so frequently been discussed that it is only the introduction of some new information derived from experimental sources that can warrant its being made the subject of this lecture. The additional facts which I propose to bring forward before you to-day have been ascertained during the past two years from experiments made by me in the Pathological Laboratory of the University of Cambridge. If they be corroborated by other investigators they will materially alter our conceptions of to-day upon the pathology of œdema.

œdema has long been recognised by the medical profession. The other name—dropsy—by which it is known is evidence etymologically of the fact; and yet the pathological explanation of the condition was not questioned until the year 1680, when Richard Lower ligatured the inferior vena, and obtained œdema of both lower extremities. From this experiment he came to the conclusion that œdema depends upon an increase of pressure in the veins, which is transmitted to the capillaries, and which leads to an increased exudation of plasma from these vessels. This view, though it was not universally accepted by Lower's contemporaries, nevertheless held its own for 200 years, when the first formidable attack upon it was made by Ranvier in 1869. Ranvier repeated Lower's experiment, but with negative results; he therefore added to ligature of the inferior vena cava section of the sciatic nerve on one side. On this side he obtained œdema, whereas in the other limb, which was equally exposed to the effect of the venous obstruction, but which was free from the effects of nerve-section, no œdema appeared. Ranvier therefore ascribed œdema to vasomotor action. A few years later Cohnheim, who investigated the subject more thoroughly than any of his predecessors, stated it as his opinion that passive œdema was the result of two antagonistic pressures: venous obstruction and arterial pressure,

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