

SOME CASES OF THYROID CARCINOMA.¹

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(PLATES LIX. AND LX.)

OF the twelve cases of thyroid tumour which I shall describe, nine have been under treatment in the wards of St. Thomas's Hospital, and by the kindness of Messrs. Clutton, Pitts, Makins, Battle, Robinson, and Wallace the clinical notes and pathological material of them have been placed at my disposal. Mr. Clutton has very kindly extended to me the same privilege in the case of two patients operated on by him in his private practice. I have, moreover, to thank Mr. Pitts for the use of the notes of one of his private cases. My thanks are due to Mr. Shattock for valuable suggestions and advice, and to Mr. L. S. Dudgeon for very great help in both the theoretical and the practical part of the work. I have also to thank Mr. George Coats, pathologist to the Royal London Ophthalmic Hospital, for his kindness in preparing the microphotographs which illustrate the tumours described. Mr. H. A. Lediard has very kindly allowed me to examine microscopic sections from his case of thyroid carcinoma with bone metastasis.

The microscope sections of the tumours were prepared in almost every case in the following manner: Small portions were cut from the tumour, after this had been washed for some hours in running water, and were then submitted to the following fluids. Salt-formalin solution (10 parts of commercial formalin in 90 parts of 1 per cent. saline solution), twenty-four hours; 90 per cent. methylated spirit, twenty-four hours; methylated spirit, twenty-four hours; absolute alcohol, three to four hours; cedar-wood oil, twenty-four hours; paraffin, twenty-four hours, the fluid being renewed about every four hours.

The blocks were then embedded in paraffin. Sections of an average thickness of $7\ \mu$ were cut with a rocking microtome, and stained with van Gieson's stain, and with hæmalum and eosin.

The cases will be divided into two classes. The first class includes eight cases, in all of which the tumours exhibited features of carcinomatous invasion. The second class comprises four cases in which, although the clinical history was not characteristic of malignant disease, yet the histological structure of the tumours was that of carcinoma.

CLASS I.

CASE 1 (under the care of Mr. Clutton).—M. J. H., female, æt. 49. When the patient first came under observation, on 21st July 1904, a swelling in the neck had been noticed for two years, and there had been difficulty in breathing for the same period. There had been no recent change in size of the

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tumour, but it had been painful for about a month. There had been difficulty in eating for five days. The swelling was situated in the left half of the thyroid gland, and was causing dyspnoea with tracheal stridor. High tracheotomy was performed the same evening by Mr. Percy Sargent, a Kœnig's tube being inserted. The patient died three weeks later. Post-mortem, the trachea was found to be compressed by a much enlarged thyroid, the upper part of which was composed of tissue resembling the normal gland, while the lower and larger part consisted of hard white new growth. The two parts were sharply marked out from one another, but were contained within a common capsule. No secondary growths were found.

Microscopic sections of the tumour (Plate LIX. Fig. 1) exhibit a portion of a colloid adenoma with part of its capsule, which is of excessive thickness and contains compressed thyroid tissue. Extending towards, and to some extent invading, this dense fibrous structure are elongated processes of squamous-celled carcinoma, many of which have a central lumen filled with cellular débris. None of the cells of the new growths show evidence of keratinisation, and no cell nests are seen. The tissue through which the epithelial processes have passed is for the most part richly cellular, but contains some dense fibrous tissue; no thyroid elements are seen in it.

The supposition that this tumour may have been of secondary origin appears to be negatived by the following considerations: The apparently healthy condition of the overlying skin, and the absence of keratinisation and of a stratum granulosum in the epithelial processes, would preclude an origin from a primary cutaneous focus; while the fact that this was the only tumour found in the body, and that there was no evidence of disease elsewhere, would render the hypothesis of an origin from a mucous membrane focus extremely improbable. Again, the manner of incorporation of the tumour in the thyroid gland, and the complete absence of lymphoid tissue, would seem to exclude the possibility of its having originated in a secondary lymphatic gland infection. Mr. Shattock is of opinion that it had its origin in the epithelium of the thyro-glossal duct, the manner of its incorporation in the gland rendering such a mode of origin more probable than one from included elements of a branchial cleft.

CASE 2 (under the care of Mr. Battle).—E. H., female, æt. 49. For two and a half years before the date of operation the patient had been noticed to be growing languid and irritable; it was said that during the same period the features had altered, and the speech had been getting slower. Eighteen months before the date of operation three small hard swellings were noticed in the neck, one in the mid-line and one at each side. The one on the right side eventually disappeared, but the other two gradually increased in size, and the anterior one became black and soft, and on the day of admission to hospital ulcerated through the skin. There was some difficulty in swallowing, and loss of flesh. At the operation, on 4th October 1899, the tumour was found to have infiltrated the neighbouring muscles, and was removed as far as possible. The removal was followed by recurrence, and six months later the lateral tumour ulcerated through the skin, considerable hæmorrhage resulting. At this time both tumours were of about the size of a lemon, the anterior one being hard and apparently fixed to the sternum, while that on the left side was soft and fluctuating. Small hard glands could be felt beneath the angles of both jaws.

The microscopic structure of the tumour removed at the operation is considerably obscured by extensive hæmorrhages and necrotic changes. The epithelial elements are comparatively scanty, and consist of large columnar cells with oval deeply staining nuclei arranged so as to form irregular alveoli into which papilliform processes covered by a similar epithelium project. No colloid material can be seen. The connective tissue is very scanty and contains few nuclei, but supports great numbers of capillary blood vessels. In parts of

the tumour calcareous deposit has occurred. The subsequent history of the case is not known.

CASE 3 (under the care of Mr. Clutton).—Miss M., æt. 52. The patient came under observation, on 19th June 1905, for a glandular mass of elastic consistence in the right side of the neck which had been noticed for twelve months, and had for six weeks been increasing rapidly in size with signs of inflammation. There had been a goitre for fifteen years, which was found to be very hard and nodular, but uniform in consistence. It moved with deglutition. There was no dyspnœa on exertion and no inspiratory stridor. Within a week of the first observation, with rest only, the glandular mass had diminished to half its original size, and had become more movable. A week later it was removed, the dissection involving the ablation of 5 in. of the internal jugular vein, to which it was intimately adherent. The operation was followed by a slight alteration in the voice, and laryngoscopic examination by Mr. H. B. Robinson revealed a subglottic growth protruding from between the vocal cords, presumably thyroid growth which had perforated the trachea. There were also early signs of paralysis of the right vocal cord. The patient regained her voice shortly after the operation, and was soon able to resume her occupation as lady's maid.

The microscopic sections (Plate LIX. Fig. 2) of lymphatic gland removed at the operation exhibit a luxuriant epithelial growth in a connective-tissue framework which is very scanty, but is rich in large nuclei. The epithelial cells are of large size and of cuboidal or columnar shape, with round or oval somewhat vesicular nuclei, and are arranged so as to enclose narrow spaces, some of simple, others of extremely complex, outline. The irregularity in outline is due to the presence of very numerous filiform intravesicular processes, formed apparently by protrusion of the vesicle walls. The spaces have for the most part no obvious contents, but in some there are traces of a thin mucinoid substance, while in a few of the smaller ones colloid material can be seen. The growth is actively invading the neighbouring tissues. Capillary blood vessels are fairly numerous. An interesting feature of the growth is the tendency exhibited in parts, side by side with obviously malignant epithelial invasion, to the formation of a connective-tissue capsule containing compressed epithelial elements, this capsule being apparently formed by the compression of the peripheral portions of the neoplasm.

In November 1905 the patient's general health was not so good as it had been shortly after operation, and on laryngoscopic examination the intralaryngeal growth was obvious.

CASE 4 (under the care of Mr. Clutton).—M. B., female, æt. 49. The patient's previous health had been good. There had been a goitre in the right side of the neck for twelve years, which had caused no inconvenience until six months previously, when the upper and rightward part of the tumour began to get larger and became painful. The pain was described as shooting upwards into the head and downwards into the arm, and was also felt in the clavicle. Morphia had been given to alleviate it. There had been some difficulty in taking food, without loss of flesh, and the patient had recently completely lost her voice. There was a large tumour in the right side of the neck, the front and inner part of which resembled ordinary goitre, and was free from pain and tenderness, while the outer and upper part was hard and extremely painful and tender. The trachea was very much pushed over towards the left. The pupil and palpebral fissure were smaller on the right side than on the left. The pharyngeal wall in the neighbourhood of the tonsil and larynx and pyriform sinus on the right side were considerably pushed inwards. The right vocal cord was not seen on phonation, and movement of the left cord was impaired. On 5th February 1904 tracheotomy was performed by Mr. Clutton, a Kocher's tube being used. Soon after the

operation the breathing became laboured, and the patient died. At the post-mortem examination Dr. Powell White reported that the trachea had been pushed over to the left by a large growth in the right lobe of the thyroid gland, which was completely encapsuled except at the upper part, where irregular growth projected through the capsule. The isthmus was elongated and the left half of the gland normal. The tumour was composed mainly of white new growth, with, in the lower and outer part, some islets of darker material, such as is usually found in parenchymatous goitres. The trachea was slightly compressed laterally just below the larynx, but was not much narrowed. There was no growth projecting into it. There were no secondary growths. One lobe of the thyroid gland showed the ordinary appearances of colloid goitre, the other that of carcinoma presenting the following histological features: Microscopically part of the tumour (Plate LIX. Fig. 3) consists of groups of cubical and columnar epithelial cells with round nuclei of varying sizes, arranged sometimes in solid masses, at others forming small alveoli, many of which contain a colloid material. These epithelial groups are aggregated into lobules, and to some extent separated from one another by a scanty connective-tissue stroma containing a few elongated nuclei of rather large size, and supporting numerous capillary blood vessels with many large nuclei in their walls. As the structure of the tumour is traced towards the capsule the epithelial arrangement is found to become more and more irregular, the alveolar formation being replaced by irregularly shaped epithelial plugs without any trace of a lumen, and single cells of various shapes and sizes. As the periphery of the tumour is reached the irregularity in shape, both of the epithelial cells and of their nuclei, and the tendency to a diffuse distribution, become more and more noticeable, while the supporting connective tissue assumes a more cellular type, many cells with large elongated nuclei being recognisable.

The capsule is of considerable thickness, and shows in its outer part atrophic epithelial cells, many of them in rows, which have evidently been included during the process of its formation.

CASE 5 (under the care of Mr. Battle).—A. W., female, *æ*t. 64. About six months before operation a swelling was noticed in the right side of the neck. It had been gradually increasing, but had given rise to no pain. The patient had some difficulty in swallowing, but had not been getting thinner. The voice had been thick for about one month. The tumour was of hardish consistence, and about three inches long and one and a half inches broad. It was free from the skin, but apparently attached to the sterno-mastoid muscle. No enlarged glands were detected. On 1st September 1897 Mr. Battle removed the growth, which was found to be connected with the thyroid isthmus, and to extend backwards between the trachea and *œ*sophagus. It was found to be of soft consistence, showing numerous small yellow areas the size of a pin's head, and was apparently completely encapsuled. Two other accessory growths were removed at the same time. The tumour was pronounced by Mr. Shattock to be a carcinoma composed of spaces filled with glandular cells and invading the surrounding tissues. The patient continued in good health for about two years after the operation, when there was a rapid recurrence, which proved fatal in April 1900. Secondary growths were found, post-mortem, in the lungs.

CASE 6 (under the care of Mr. Pitts).—Notes received from Mr. Pitts, September 1905.—E. B., female, *æ*t. 47. Married. One child, stillborn. Five years ago a small swelling was noticed in the centre of the neck, associated with difficulty in breathing and with nocturnal dyspnœic attacks. A few months later the tumour was removed by another surgeon, and was pronounced to be a carcinoma of the thyroid gland containing a large amount of fibrous tissue. Since then an operation has been performed every year for the removal of tumours in the lymphatic glands of the neck, which exhibited

a structure identical with that of the original tumour. One year ago the patient began to experience sharp pain in the left leg, and during the last six months she has suffered severely from this, the pain being only relieved by morphia. There has been considerable loss of flesh and failure of strength. There is now a well-marked fusiform swelling of the lower end of the left femur, which is tender on pressure. A number of small glands can be felt in the neck.

CASE 7 (under the care of Mr. Clutton).—Mrs. V. Attached to the right side of the cricoid cartilage was a small smooth elastic body, which moved with deglutition. The tumour had been noticed for six weeks at the time of operation. On 19th June 1905 it was removed, and was found to be a small growth directly continuous with the thyroid gland. The microscopic sections (Plate LX. Fig. 4) show the tumour to consist for the most part of tissue almost precisely similar to that met with in the normal thyroid gland, namely, colloid-containing vesicles of various sizes and forms lined by a single layer of perfectly regular cubical or somewhat flattened epithelium, together with some smaller solid epithelial masses. The colloid material is somewhat vacuolated. The connective tissue in which these epithelial elements are embedded is of fibrous character with a few elongated nuclei, and is more abundant and of looser texture than that met with in the normal gland. Blood vessels are numerous and well formed. At various points in the sections can be seen bundles of striped muscle fibres, many of which are shrunken and atrophic, completely surrounded by the new growth. Elsewhere may be seen small compressed vesicles with atrophic lining epithelium and thin contents. These are most evident amongst the muscle fibres, and are apparently portions of growth which have penetrated the muscle bundles, but whose vitality has subsequently suffered. There was no evidence of recurrence of the growth fourteen weeks after operation.

Case 8 (under the care of Mr. Battle).—S. S., female, æt. 64. Six years before the date of operation, 16th March 1900, a small hard lump had been noticed in the right side of the neck, about two inches above the clavicle. This had increased gradually for five years, and growth had then become more rapid. A swelling had been observed in the mid-line of the neck for six months, and a swelling in the left side of the neck for a week. There had been no difficulty in swallowing, but some difficulty in breathing for three months. The patient had been losing flesh for twelve months. The swelling in the right side of the neck was about as large as an orange, and presented a small fluctuating eminence on its surface. It was movable on the subjacent tissues, but did not move with deglutition. The swelling in the mid-line was about the size of a walnut, of hard consistence, and moved with the larynx. There was a hard swelling in the left side of the neck which did not move with deglutition, but was movable on the subjacent tissues. At the operation Mr. Battle found that one tumour was very intimately connected with the trachea. It was detached with some difficulty, and was found on section to be cystic. The base of the tumour was indurated, and from it a cauliflower-like papilliform growth was springing. Four days later the breathing became greatly embarrassed, and tracheotomy was performed. The patient died a week later. Microscopic examination of the tumour shows in the more central parts a very scanty supporting connective tissue in which are epithelial cells, arranged in some cases in solid groups, in other cases forming the lining walls of colloid-containing cavities, circular, oval, or elongated in outline. The lining cells are of cubical form and regular arrangement, and have large round nuclei, staining as in normal thyroid tissue. Towards the periphery of the tumour the epithelial cells exhibit less regular outlines, while their nuclei are in many cases of large size and oval shape. The cells are disposed almost entirely in solid masses, and are invading the dense fibrous tissue in their neighbourhood.

CLASS II.

In the group of four cases to be next described, although the clinical history in all would seem to negative the view that the patients were victims of malignant disease, yet the microscopic structure of the tumours removed was pronounced by Mr. Shattock to be that of carcinoma. The tumour capsule, in the two cases in which it could be microscopically examined, showed no evidence of epithelial invasion.

CASE 9 (under the care of Mr. Makins).—A. N., female, *æt.* 32. At the time of operation a tumour had been noticed in the anterior and left parts of the root of the neck for eight years. It was said to have increased for four years, and then to have diminished in size; while recently it had varied in size from day to day. The tumour was about the size of a turkey's egg, soft and elastic, and moved with deglutition. The right side of the neck was fuller than normal, but no definite tumour could be felt. There was no obvious dyspnoea. On 8th May 1905 the tumour was enucleated by Mr. Makins. It was definitely encapsulated, rather pale and yellow in appearance, and homogeneous in structure. Convalescence was uneventful. Microscopic examination shows the tumour in this case (Plate LX. Fig. 5) to be composed of epithelial cells with granular cytoplasm and large round or oval somewhat vesicular nuclei disposed in an oedematous connective tissue with few and elongated nuclei and of finely fibrillated texture. The proportion of epithelium to connective tissue varies in different parts of the tumour. Immediately beneath the capsule, which is composed of fibrous tissue, between the layers of which may be seen atrophic-looking epithelial cells disposed both singly and in rows, the growth is composed almost entirely of solid columns of large polyhedral epithelial cells with well-formed nuclei, separated by a very scanty connective tissue. As the section is traced inwards the connective tissue becomes somewhat more evident and of looser texture, and a few small circular alveoli lined by epithelium of degenerate appearance with flattened nuclei and containing vacuolated colloid material may be seen scattered at wide intervals amongst the other epithelial elements. The relative proportion of connective tissue to epithelium, and the looseness in texture of the former, are found to increase as the section is traced still farther from the capsule, and at the same time the disposition of the epithelial cells is seen to become more and more irregular. Arterioles are numerous and capillaries are present in enormous numbers, the epithelial cells resting in most cases directly on their walls. At many points in the sections the connective-tissue fibrillæ appear to be intimately connected with the capillary endothelium. At no point in the section is there any evidence of invasion of the capsule by the epithelial cells. In July 1907 the patient wrote to say that she was in excellent health.

CASE 10 (under the care of Mr. Cuthbert Wallace).—C. W. T., male, *æt.* 40. A swelling in the lower part of the neck was first noticed about ten weeks before operation, and during this period it had doubled in size. There had been no pain and no difficulty in swallowing.

The swelling extended downwards to within about $\frac{1}{4}$ inch of the sternum, forwards just across the middle-line, and backwards beneath the sternomastoid muscle. It moved with deglutition, was of elastic consistence, and was not tender. In August 1905 Mr. Wallace removed the tumour, which was found to involve the whole of the left lobe of the thyroid gland, and to be of very friable consistence. There was no tumour capsule, and the gland capsule was not removed. Convalescence was normal. Histologically the

tumour in this case consists of groups of epithelial cells separated by a hyaline connective tissue which contains only a few elongated nuclei. The epithelial cells are of smaller size than those in the tumour last described, and appear either as polyhedral cells arranged in solid groups and columns or as subcolumnar cells surrounding small spaces containing a material like turbid colloid. Stained with hæmalum and eosin the cells appear to be of two types:—

1. Cells with round fairly deeply staining blue nuclei, and much vacuolated cytoplasm staining a faint blue, and

2. Cells with round or oval deeply staining port wine nuclei and pink homogeneous protoplasm. Many intermediate types are also present. There are also some larger empty spaces devoid of contents and surrounded by flattened cells with elongated nuclei. Capillary blood vessels with large elongated nuclei in their walls are numerous. It is to be noted that histologically the epithelial structure of this tumour bore some resemblance to that obtaining in the normal parathyroid body. In July 1907 there had been no recurrence of the tumour, and the patient was in good health.

CASE 11 (under the care of Mr. Pitts).—L. P., female, æt. 28. The patient had always realised that her neck was large, but this had been more noticeable for the eleven years preceding operation. There had always been slight difficulty in breathing, which was more pronounced on exertion and in damp weather. There had been no difficulty in swallowing. A cystic adenoma of the left ovary had been removed a month previously. There was fulness in the thyroid region. In the position of the isthmus a distinct firm lump could be felt which moved with deglutition. On 16th December 1903 Mr. Pitts removed a tumour which involved the thyroid isthmus and the entire left lobe. It passed deeply and pressed chiefly on the left side of the trachea, which was flattened from side to side. Convalescence was normal.

Microscopic sections showed the presence of multiple cystic adenomata in the left lobe of the gland. The tumour found in the isthmus (Plate LX. Fig. 6) consists of a finely fibrillar connective tissue forming alveoli, in which are seen epithelial cells with large rather deeply staining nuclei and granular protoplasm. Many of the cells are of polyhedral shape, and are disposed in solid groups and tortuous columns devoid of all semblance to glandular formation; others, again, are of subcolumnar form, and enclose tubular and circular spaces of varying calibre. The contents of these spaces and tubes in some cases resemble a much vacuolated colloid, but in most instances consist of a coarsely granular material of degenerate appearance. The connective tissue, is oedematous, and varies considerably in amount at different parts of the tumour. Calcareous deposits are present in some parts of the tumour. The connective-tissue nuclei are few in number, and are situated almost entirely in the rings of tissue immediately surrounding the epithelial cells. Capillary blood vessels are very numerous. In July 1907 there had been no recurrence of the tumour, and the patient was in excellent health.

CASE 12 (under the care of Mr. H. B. Robinson).—J. S., female, æt. 34. For three years before operation a small swelling had been present in the neck. During the same period there had been occasional pain in the region of the heart and a dry cough. There had been difficulty in swallowing solid food, and dyspnœa, especially during recumbency, for a year. At the time of operation, 6th January 1905, there was a tumour about the size of a hen's egg in the middle-line of the neck immediately above the sternum. The swelling moved with deglutition and was not attached to the skin. The tumour was enucleated by Mr. Robinson, and proved to be of pale grey colour. It was situated in the right half of the thyroid isthmus, and had patches of normal thyroid tissue around it. There were several cystic cavities within it with thin blood-stained contents. Convalescence was normal.

Microscopic sections of the tumour in this case (Plate LX. Fig. 7) are remarkable in two respects, the extraordinary irregularity of the epithelial growth and the great amount of connective tissue present. The latter is of finely fibrillated structure, and is at some points of loose texture, while at others it is extremely dense. It contains but few nuclei, and these are for the most part situated immediately in relation with the epithelial cells embedded in it. The latter consist of granular cytoplasm with large round or oval fairly deeply staining nuclei, and exhibit an extraordinary variety of form and arrangement. Many of them are of very irregular shape, and are distributed through the stroma with the utmost abandon, in formations which show no tendency to conform to type. Others again are aggregated into solid groups of circular or oval outline. At other points are similar groups with a small central lumen, and in some places definite spaces of various forms and sizes, some of which contain a vacuolated colloid material, may be seen. Capillary blood vessels are fairly numerous, and the tumour has been the seat of extensive hæmorrhages. The capsule is composed of many layers of fibrous tissue, and at some points compressed epithelial elements are seen between these layers; there is, however, no evidence of active epithelial invasion. The patient wrote, in July 1907, to say that she was in very good health, and free from all symptoms of her former disease.

In a thesis published in 1889 Orcel observes that the thyroid tumours which appertain to the embryonic forms are those recognised clinically as malignant; the adult forms constitute the benign. Woelfler (1879) maintains that the only difference which exists between the adenoma and the carcinoma lies in the enormous power of proliferation of the cells of the latter, and the absence of any tendency in carcinomatous tissue to organise itself in the appearance of normal thyroid tissue.

These statements, although containing much that is true, are nevertheless open to criticism. Thus a study of the structure of the tumour in Case 7 makes it clear that the epithelial cells of a carcinoma may reproduce structures which are histologically almost indistinguishable from adult gland tissue; furthermore, there is strong evidence that carcinomatous tumours may reproduce the internal secretion proper to the normal thyroid gland. On the other hand, it is not rare to meet with encapsulated epithelial tumours which are free from all suspicion of malignancy, but in which much of the epithelium is essentially embryonic in character, and shows but little tendency to conform to typical arrangement. It seems necessary, therefore, to modify the views enunciated by Orcel and Woelfler by a recognition that the presence of glandular tissue of adult type cannot invariably be accepted as excluding a malignant character, while the existence of embryonic tissue can be accepted as an indication of malignancy only when it is present in atypical arrangement, and shows a complete absence of all disposition to develop into glandular structures.

With the question of encapsulation are connected some points of interest. I have examined a considerable number of sections of adenomata, in all of which the capsule appears to be constituted

on the same plan. The most obvious feature is a groundwork of fibrous tissue arranged in concentric bundles. Between these may be seen, here and there, epithelial elements more or less atrophied, in some places in the shape of elongated vesicles containing thin colloid and lined by flattened cells, in others in the form of somewhat shrunken cells often disposed in rows, the arrangement in all cases being in conformity with the longitudinal axis of the fibrous strands. The formation of the capsule appears to be due to an excessive development of connective tissue in the peripheral parts of the tumour, and the subsequent compression of these parts together with the surrounding normal gland tissue as a result of the continued growth of the more central parts of the tumour, the pressure leading eventually to atrophy of the epithelial elements. An exactly similar process may often be observed in the interior of the tumour as the result of focal growth.

That the capsule is to some extent formed by new tissue the result of excessive connective-tissue proliferation at the margin of the tumour, and not solely by compressed adenomatous and normal tissues, is suggested by the observation that in the capsule the proportion of fibrous tissue to epithelial cells is considerably higher than that which obtains in either normal thyroid tissue or adenomata.

With the fact that epithelial cells are to be found included in the capsule of adenomatous tumours is related a point of considerable practical importance; inasmuch as it is not impossible for such cells to be mistaken on microscopic examination for cells of the tumour invading the capsule from within. This mistake may usually be obviated by bearing in mind that cells included during the process of capsule formation are generally of more or less atrophic character, and definitely isolated from the body of the tumour; while their arrangement is strictly in accordance with the lamination of the capsule. Moreover, seeing that cells of the tumour are included within the inner layers of the capsule, it would seem possible that these may in some cases be responsible for the reappearance of an adenomatous tumour after an apparently successful enucleation. Although true invasion of the capsule by epithelial growth is to be regarded as strong evidence of malignancy, yet the presence of a capsule which on microscopic examination is quite free from such invasion and appears in all respects identical with that met with in an adenoma cannot be accepted as proof of innocence of the growth. Such a capsule was seen in microscope sections from Cases 9 and 12 in Class II. and from Case 4 in Class I., although in the latter case the tumour presented at other parts macroscopic evidence of invasion of surrounding tissues. These histological appearances are in accord with the unanimous observations of authors as to the frequency in the case of thyroid tumours of the precedence of a carcinomatous by an innocent growth.

As to the influences concerned in the genesis and type of formation of carcinomatous thyroid tumours it is perhaps somewhat hazardous to speculate. Mr. Shattock has suggested to me, in view of the frequency with which adenomatous thyroid tumours are met with in patients at a period of life in which there is likely to be a special call on the products of glandular activity, that the origin of these tumours may be a manifestation of a response to such a demand, and this suggestion is strengthened by a specimen of a child's liver in his possession which exhibits, in association with cirrhotic changes, newly formed masses of functional liver cells. On this supposition the young cells exhibiting rapid growth met with *par excellence* in the foetal type of adenoma would be strictly analogous to the cells of similar type met with in rapidly growing parenchymatous goitre. The evidence afforded by von Bergmann's cases that malignant thyroid tumours may, in some cases at all events, perform a physiological function is suggestive that perhaps here also a physiological demand may exert some influence on the genesis and structure of the tumour.

In only two of the cases reported above was there evidence of tumour metastasis, and in one of these (Group I. Case 6) the evidence was conjectural. Ten cases which appear to illustrate this complication have been recorded in English literature by Caesar Hawkins (1843), Wilson Brown (1844), Henry Morris (1878), Warrington Haward (1882), R. E. Carrington (1885), Joseph Coats (1886), R. G. Hebb (1888), Edgar Willett (1891), and H. A. Lediard (1903). In continental countries the complication would appear to be a common one. Thus Ehrhardt (1902) states that in ninety-four bodies examined metastases were found in all but fourteen; and R. Jaeger (1897), under the title of Goitre-metastasis, has reported twenty-six cases of metastatic thyroid tumour. An analysis of the thirty-six cases referred to above, and of one case described by Billroth (1881), gives the following results as to the site of metastasis:—

Site of Metastasis.	
Multiple bone	11 cases.
Single bone	18 „
Skull	17 „
Spine	8 „
Humerus	6 „
Pelvis	5 „
Femur	3 „
Lower jaw	3 „
Sternum	1 case.
Ribs	1 „
Clavicle	1 „
Scapula	1 „
Lung	9 cases.
Lymphatic gland	3 „
Bone and lung	4 „
Bone and lymphatic gland	1 case.

Lung and lymphatic gland	1 case.
Kidney	4 cases.
Liver	3 „
Spleen	1 case.
Omentum	1 „

The distribution of the metastases makes it evident that the cancerous emboli pass to their destination by the blood stream, and also points to direct entrance through the wall of a blood vessel being of much commoner occurrence than an indirect route by the lymphatic circulation. The frequency with which hæmorrhages are met with in these tumours lends support to the view that the rupture of vessels under the influence of slight injury or severe strain is of no uncommon occurrence, and in this way a ready means of entrance into the circulation would be afforded to growing cells.

The slow rate of growth of bone metastases is often very noteworthy, and is well illustrated by some of Jaeger's cases. Von Eiselsberg has pointed out that these secondary deposits may apparently have the power of producing sufficient thyroid secretion to fulfil the requirements of the organism; in a case under his care cachexia strumipriva, which set in after total excision of the thyroid gland for adenomata, was observed to abate with the growth of a sternal tumour, the removal of which six years later was followed by post-operative tetany. The tumour was found to consist entirely of cylindrical-celled carcinoma with the power of secreting colloid.

CONCLUSIONS.

1. That thyroid carcinoma is not so rare a disease as is generally supposed.
2. That while, on the one hand, epithelium of atypical character and arrangement is not infrequently met with in thyroid adenoma, thyroid tissue of adult structure may be encountered in carcinoma.
3. That the presence of a tumour capsule identical with that found in thyroid adenoma may be met with in the case of carcinomatous tumours.
4. That it is important in microscopic examination of thyroid tumours not to mistake epithelial cells which have been included in the capsule during the process of its formation for cells invading it from within.
5. That thyroid carcinoma is very frequently the manifestation of a change in type of an apparently innocent encapsulated tumour, a fact which will reinforce other indications for the removal of a tumour of this character.
6. That the disease not infrequently pursues a more protracted course, and is more amenable to surgical treatment, than is generally supposed.

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DESCRIPTION OF PLATES LIX. AND LX.

PLATE LIX.

- FIG. 1.—Tumour in Case 1. ($\times 35$.)
- FIG. 2.—Tumour in Case 3. ($\times 120$.)
- FIG. 3.—Tumour in Case 4. ($\times 120$.)

PLATE LX.

- FIG. 4.—Tumour in Case 7. ($\times 120$.)
- FIG. 5.—Tumour in Case 9. ($\times 120$.)
- FIG. 6.—Tumour in Case 11. ($\times 120$.)
- FIG. 7.—Tumour in Case 12. ($\times 120$.)

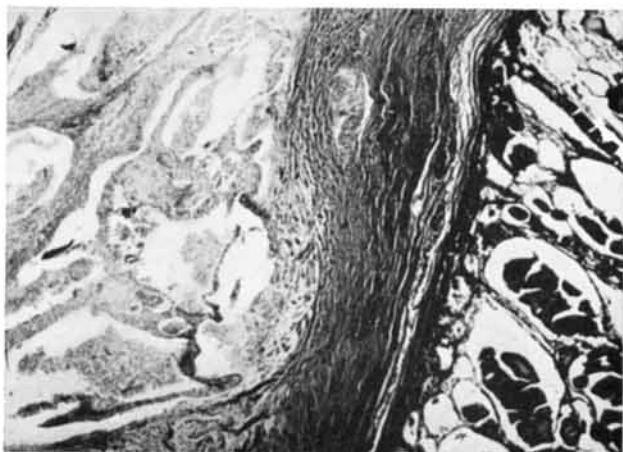


Fig. 1.

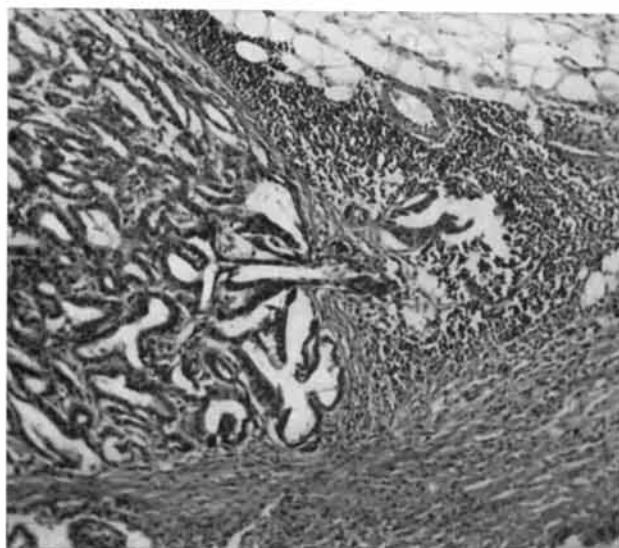


Fig. 2.

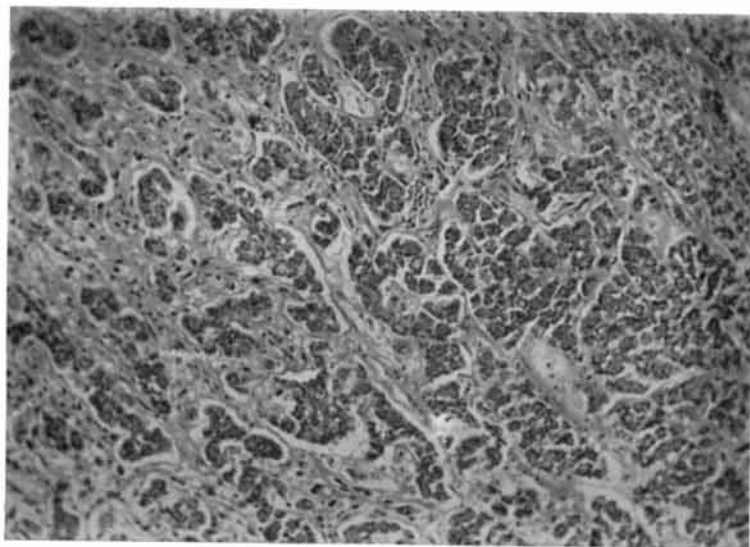


Fig. 3.

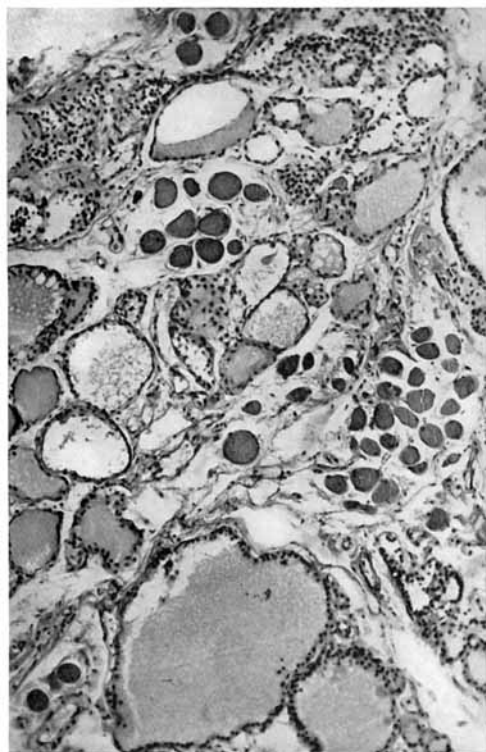


Fig. 4.

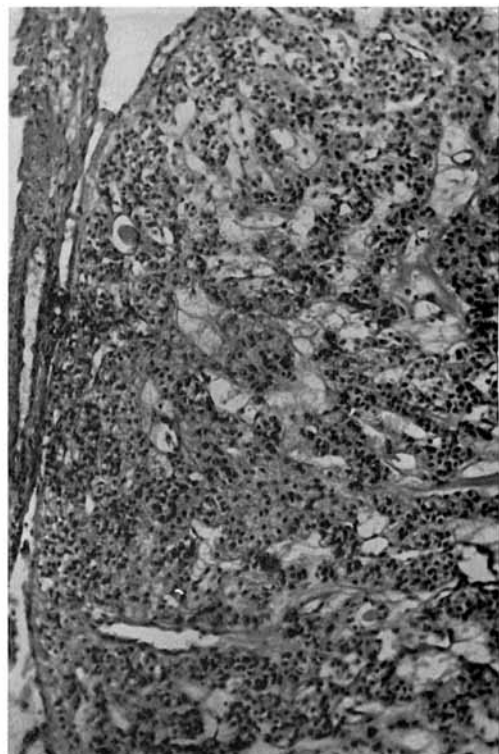


Fig. 5.

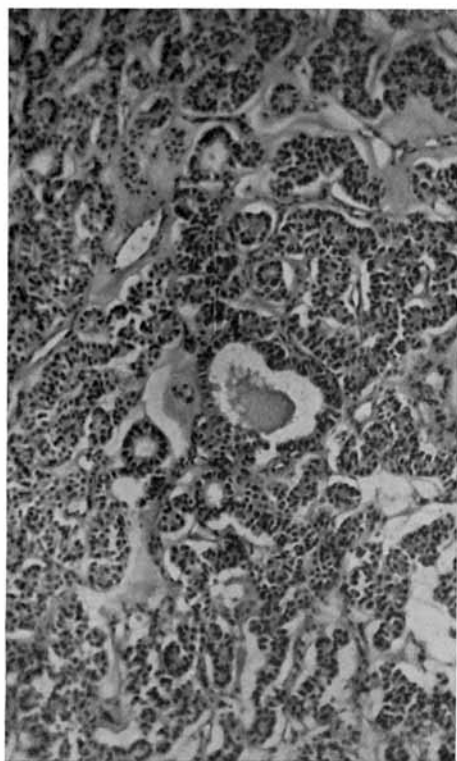


Fig. 6.

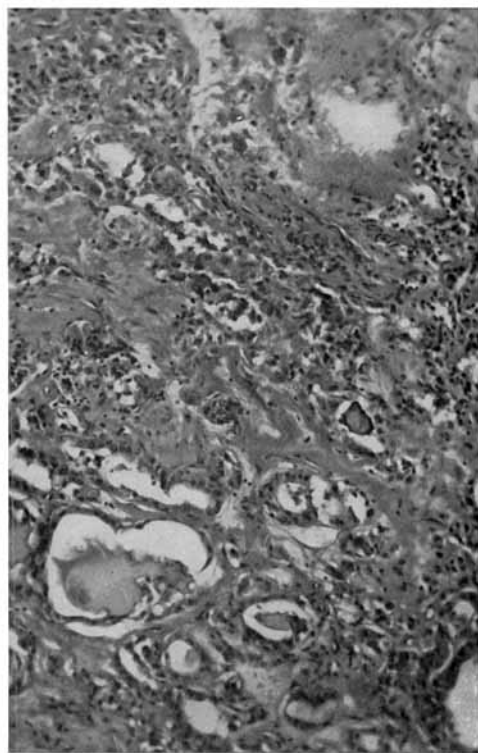


Fig. 7.