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CASES OF PRIMARY CARCINOMA OF  
THE APPENDIX VERMIFORMIS

BY

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*(From the Pathological Department of the Glasgow Royal Infirmary.)*

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## CASES OF PRIMARY CARCINOMA OF THE APPENDIX VERMIFORMIS.

CASES of carcinoma of the appendix have always been considered of very great rarity, and, while admittedly they are rare, the number on record is steadily increasing with the custom of having all appendices removed at operation submitted to microscopical examination. From their situation they give rise to symptoms which direct attention to the appendix, and its early removal, preventing metastasis, goes a long way to explain the apparent non-malignancy of this tumour, which recently has been stated to be in the majority of cases a simple form of endothelioma.

In THE LANCET of Oct. 23rd, 1909, I reported a case of primary carcinoma of the appendix in a man, 49 years of age. This patient remained in good health without return of any symptoms, and ten months after his operation left for Canada, reporting himself by letter, a month later, quite well. The specimen was found in the routine histological examination of appendices removed at operation. Since then I examined microscopically in the same way 40 appendices before I found the first of the two primary cases now reported. In this new case the appendix is constricted and the lumen occluded, the carcinoma arising at the site of the occlusion.

CASE 1.—The patient is a particularly healthy-looking young woman with a florid complexion. She is only 23 years of age. In November, 1908, she had her first attack of appendicitis; she was seized with sickness and vomiting which continued for about two days, and, shortly after the commencement of the sickness, severe pain in the right iliac region. The attack lasted three weeks. In November, 1909, she had a second attack similar in nature, but less severe than the first. Since her first attack she had always felt a little uneasiness or tenderness in her appendix region, more particularly when she had walked for some time. For three or four years previous to her first attack she had been subject to "bilious attacks," but, except for attacks of measles and scarlet fever, she had always enjoyed good health.

The patient was admitted to Mr. P. Paterson's wards at the Glasgow Royal Infirmary on May 6th, 1910, for operation in the quiescent period after her second attack. Examination revealed tenderness on pressure over the appendix region, but there was no distension of the abdomen nor rigidity of the recti muscles. On May 9th Mr. Paterson performed appendicectomy, and although the organ was readily removed it was found to be adherent to intestine in places.

Mr. Paterson states that at the operation there was nothing found which in any way suggested to him the presence of malignant disease in the appendix or its neighbourhood. The appendix measured  $2\frac{1}{4}$  inches in length, and on external examination it was apparent that there was a constriction  $\frac{7}{8}$  inch from the distal end. The distal segment formed a spindle-shaped swelling; the proximal segment is narrower and cylindrical. The whole appendix was fixed in formalin 5 per cent., and, after washing, was divided longitudinally in the axis of the meso-appendix. On examining the cut surfaces it was at once seen that the external constricting marking corresponded to a definite stricture of the lumen, apparently a complete occlusion. This appeared to be produced by a thickening of the submucous layer and folding inwards of the mucous membrane, which was limited to the side of the appendix opposite its mesenteric attachment. The distal segment showed a uniform distension of its lumen with a creamy substance which proved to be pus. Nothing of note was apparent to the naked eye in the proximal segment.

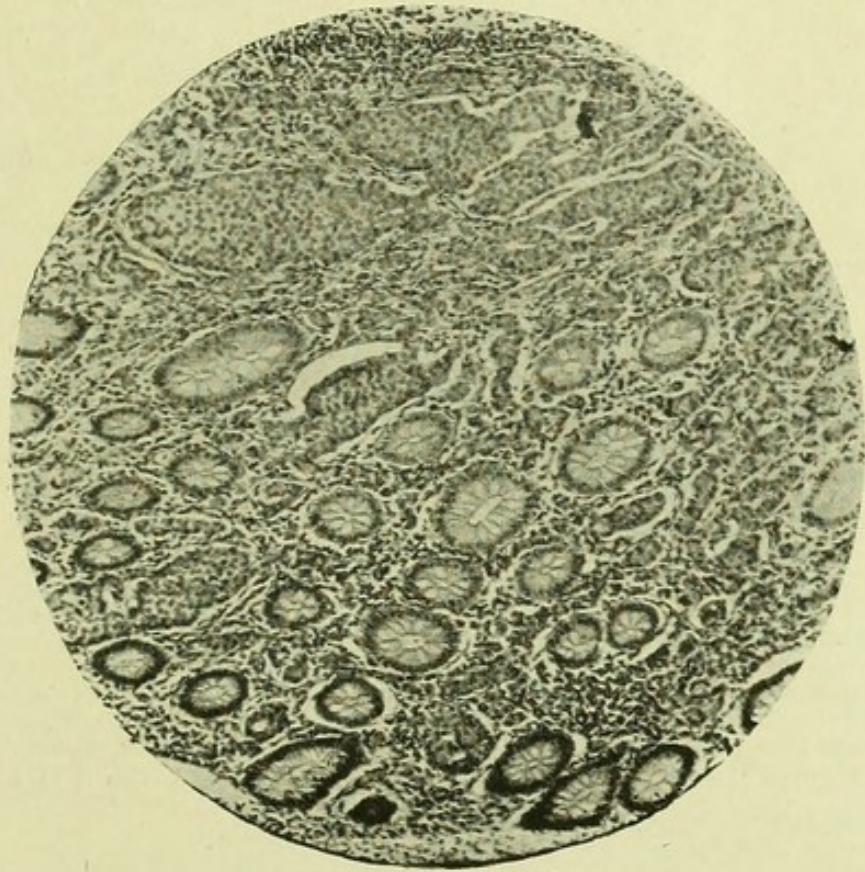
*Microscopical examination of appendix.*—A portion about half an inch long was taken, and longitudinal sections were cut from it; this portion was taken from about the centre so as to include the occluded portion and part of the appendix on either side of it.

The lumen distal to the constriction is dilated and contains inspissated pus, and there is some flattening of the mucous membrane. Proximally the lumen contains only a little mucus and blood, the latter probably the result of the operation. Throughout, for the greater part, there is a fairly uniform thickening of the submucous fibrous layer. At the site of the occlusion this layer is seen to thicken on the side opposite to the mesenteric attachment and then dip in and pass across the lumen, as a narrow band, to the opposite side. The mucous membrane on either side turns inwards and lines the constriction. The circular muscular layer also bends inwards for a short distance at this point.

In this constricted area, and limited to the part of the appendix opposite the mesentery, is an unmistakable carcinoma. In the mucous membrane adjacent to the distal side of the occlusion the carcinoma is seen extending from about midway across the lumen towards the peritoneum. In the mucous membrane carcinoma cells lie side by side with the normal glands, and apparently replace others. (Fig. 1.) The cells are fairly large, spheroidal, with relatively large nuclei, arranged in the alveoli of a scanty fibrous stroma, and forming solid masses of varying size. In short, the structure is that of a typical scirrhous carcinoma.

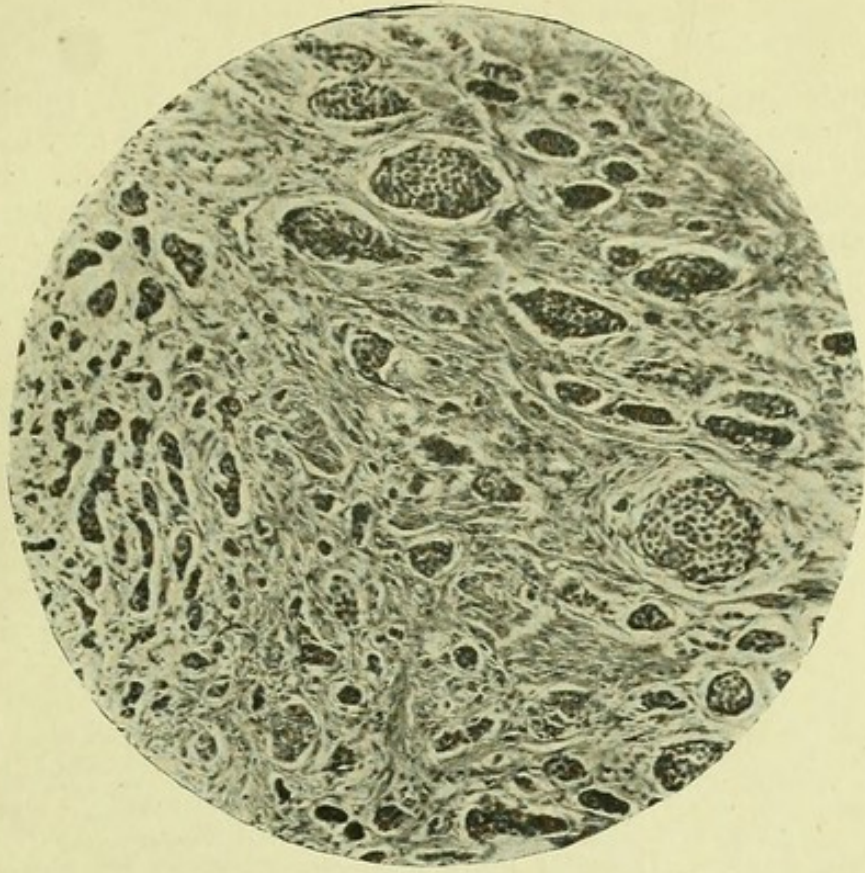
Passing from the mucous membrane outwards, the carcinoma is seen in the greatly thickened portion of the submucous coat as numerous smaller masses of epithelial cells in the alveoli of a much more abundant fibrous stroma. It passes through the circular muscular coat as a few isolated masses between the muscle fibres. When it reaches the longitudinal layer of muscle it again forms a definite collection of similar solid masses of epithelial cells arranged as before, in the alveoli of a dense and fairly abundant fibrous stroma. (Fig. 2.) The tumour extends outwards to the peritoneal coat, which is thickened and covered with old adhesions.

FIG. 1.



Carcinoma of appendix.  $\times 90$ .

FIG. 2.



Carcinoma of appendix.  $\times 90$ .



Immediately beyond the constriction, adjacent to the carcinoma, there is a deep acute ulcer filled with pus, and extending almost right through the mucous membrane. The muscular coats beneath this ulcer are lost, their place being taken by the old adhesions already noted over the tumour. It appears very probable that this defect in the muscular coats and the formation of adhesions, together with the occlusion, are the result of a former ulceration of the appendix wall. Further, in this occluded area and, as yet, limited to it, there is now present an unmistakable scirrhous carcinoma. There is nothing further of note in the appendix beyond the fact that throughout the circular muscular layer there is considerable fatty degeneration.

The second new specimen was found post mortem, without the appendix having previously been suspected. In it also the appendix is constricted and occluded a short distance from its tip, which is bulbous and occupied by tumour.

**CASE 2.**—The patient was an extremely emaciated woman, aged 42 years, who was admitted to the medical wards of the Glasgow Royal Infirmary suffering from hepatic enlargement with ascites, and later was transferred to the surgical wards for abdominal drainage. She had been a heavy drinker for many years and had long suffered from indigestion after practically every meal. She had ascites for six months, and œdema of the legs for three months, before admission. On admission there was constant pain over the whole upper and left side of the abdomen, but she was unable to point to any one spot as being the site of greatest pain. The pain was sharp and stabbing and frequently very severe. She died suddenly a month after the operation.

*Necropsy.*—At the post-mortem examination the liver was found enormously enlarged (129 ounces), and showed an extreme degree of amyloid degeneration, with thickening of its capsule. The spleen and kidneys were also diffusely amyloid, and the capsule of the former was thickened. A firm fibrous mass of thickened adherent pleura, with a large cicatrix in the left lung under it, was found; it was evidently very old, and nothing was found anywhere else in the lung indicative of its nature. There had been a chronic peritonitis, evidenced by thickening and opacity of the peritoneum, with adhesions throughout the abdomen. The stomach and intestine throughout presented an œdematous condition but no other sign of disease.

The appendix was shorter than usual, turned back upon itself, and adherent to the adjacent loop of small intestine. On separation, it was seen that the tip of the appendix was occupied by a small hard nodule, the organ being club-shaped. Careful search was made, but no other tumour nor enlarged glands were found.

*Microscopical examination of appendix.*—The appendix was fixed in formalin, and longitudinal sections of the whole organ, in addition to transverse sections of the tumour, were prepared. The tip of the appendix was demarcated from the remainder and bent inwards towards the meso-appendix, and in it there was present a carcinoma.

There were old adhesions round the appendix, and the muscular coats showed some fibrosis. There was considerable thickening of the

submucous fibrous coat throughout, and the mucous membrane was also thickened and fibrosed. About  $\frac{3}{8}$  inch from the tip the appendix is completely occluded. Here sections show the circular muscular layer extending right across the organ, bounded on either side by the thickened layer of submucous fibrous tissue. On the mesenteric side the longitudinal layer of muscle dips inwards for a short distance at the site of occlusion, but on the opposite side it passes right over and round the tip.

Beyond the occlusion there is no lumen; the mucous membrane is altogether lost, and its place and the cavity are occupied by a characteristic carcinoma. The tumour appears as two nodules. One, immediately adjacent to the occlusion above mentioned, is completely surrounded by a thickened layer of submucous tissue, and apparently replaces the mucous membrane. The other is situated distally, nearer the tip, which, as above noted, is turned round towards the mesenteric attachment, and is surrounded by muscular and fibrous tissue. Externally the longitudinal and circular muscular layers are distinct, and the tumour here also is situated within a layer of fibrous tissue corresponding to the submucous coat. Between these two nodules a layer of muscle corresponding to the circular layer is present; it is infiltrated with tumour, and the infiltration extends in the circular muscular layer on either side of the distal nodule, but does not involve the tip.

The cells are spheroidal, the protoplasm is abundant, and the nuclei are relatively large and dense; they form solid masses, surrounded by a dense though rather scanty fibrous stroma. The two nodules have practically the same characteristics, and are undoubtedly scirrhus carcinoma. Between the two nodules, and spreading laterally, masses of similar cells are seen between the fibres of the circular layer of muscle.

During the past 11 months I have examined, as a matter of routine, the appendix in over 350 necropsies, yet this last case is the only primary tumour I have yet found in it. I have twice found secondary tumours in it, and in both cases they were carcinomata secondary to carcinomata of the stomach. They each showed the same structure as the primary growth in the stomach.

The three primary carcinomata of the appendix which I have now reported present features so similar as regards their site of origin that they are of considerable interest in view of the question of the etiology of tumours in general. In the first case the appendix was divided into two segments, no doubt the result of cicatrisation of previous ulceration, and in the sequestered distal portion the carcinoma was situated. In the second case there is a complete occlusion of the lumen, in all probability due to the same cause, and in this constricted area, and as yet limited to it, the carcinoma is present. In the third case the appendix is also completely occluded in the same way near its tip, and beyond the occlusion, filling up the cavity and replacing the mucous membrane, is the carcinoma.

In the first two cases, and probably in the third also, the

patient had had more than one attack of ordinary appendicitis; from the histological appearances we can conclude that it is highly probable that in each case a certain amount of localised ulceration of at least the mucous membrane occurred, followed by cicatrisation in the process of healing. No doubt this causes considerable disturbance and separation of the epithelial cells of the mucous membrane, and in each of these cases a carcinoma has arisen at the situation of the damage.

As previously pointed out, these cases are of considerable interest in view of Ribbert's theory of tumour formation—viz., that tumours arise from a partial or complete separation of cells, or groups of cells, from their organic continuity—that is to say, from mechanical isolation.

Glasgow.

