

leucos. 40,000 per c.mm. *Differential count*: Polys. 90%; lymphos. 7%; monos. 2%; eosinos. 1%. Blood platelets much reduced, less than 5,000 per c.mm. (normal 500,000 per c.mm.).

*Comment.*—This is the blood picture of essential thrombocytopenia.

*Autopsy.*—The body was thin and slightly yellow in appearance. Numerous purpuric patches were present on the skin. The tissues appeared healthy in the region of the colostomy and perineal wound. There was no free fluid in the abdominal cavity and no sign of peritonitis. Purpuric patches were noticed on the peritoneal surface of the intestines and bladder. The spleen was normal. The liver weighed 8 lb. 12 ounces. Its cut surface was pale and fatty. There were no metastases in the liver from the rectal carcinoma. The pancreas was normal in appearance. Both suprarenal glands were slightly enlarged, but otherwise normal. Blood was found in the stomach and intestine and purpuric patches were present in the mucous membrane. The kidneys showed subcapsular purpuric patches and the renal pelvis and calices were filled with blood; both ureters were completely filled with clot. The mucosal surface of the renal pelvis was stained dark brown in large irregular patches. The bladder was greatly distended and contained a large loose blood-clot. There was no sign of sepsis round the perineal wound or in the tissues of the pelvis. The heart and lungs were normal. The blood in the heart and large vessels was unclotted except in the pulmonary artery, where a loose post-mortem chicken-fat clot was found.

*Cause of death*: Death was due to renal hæmorrhage secondary to purpura caused by platelet deficiency (essential thrombocytopenia).

*Comment.*—It would seem that the carcinoma and the operation for its removal had very little to do with the onset of the condition. There was no previous history of purpura though one may suspect the epistaxis and menorrhagia as having been of the same nature.

I feel sure that nothing could have been done to prevent a fatal issue as the urinary tract was completely disorganized by the hæmorrhage, as can be seen in the specimens. The patient died from uræmia and not directly from hæmorrhage.

## Ossification in Rectal Cancer

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To meet with spicules of bone within the centre of a cancer of the intestine is surprising. It has fallen to my lot four times. In two of the cases areas of ossification were discovered within a primary rectal carcinoma, once in cancer of the pelvic colon, and in the fourth case within a recurrence from rectal cancer situated between the rectum and sacrum. These are the only cases which have been met with amongst more than a thousand excisions, so that one may say that the incidence of ossification in rectal cancer is less than 0.4%. I have not been able to find any instance of ossification in a primary carcinoma of the rectum recorded in the literature, but a case of ossification in a recurrence from rectal cancer has been previously reported (Dukes, Morgan, and Gordon-Watson, 1928).

I am recording these cases now partly because they are of interest as curiosities and partly because they exhibit certain common features which may give a clue

to the understanding of this peculiar phenomenon. These common features are : (1) Long duration of symptoms indicating slow growth of the tumour. (2) The histological picture of a growth of low-grade malignancy with no tendency to spread by veins or lymphatics. (3) The presence of areas of necrosis within the tumour.

*Case 1.*—The patient was a male, aged 69, under the care of Mr. Lockhart-Mummery. He had complained of rectal symptoms for five years and a hard protuberant tumour was found in the rectal ampulla. This was removed by perineal excision of the rectum on July 9, 1926. Examination of the operation specimen revealed a shallow ulcer about 3 in. in diameter almost completely encircling the rectum. From the central region of this ulcer a hard greyish-white tumour about 2 in. in diameter projected forwards (fig. 1). Little spicules of bone could be felt within this projecting tumour and were easily demonstrated by cutting into the growth. Microscopic examination showed the growth to be an adenocarcinoma of a very low grade of malignancy (Grade I). The sections removed from the ulcerated edge did not reveal any unusual feature

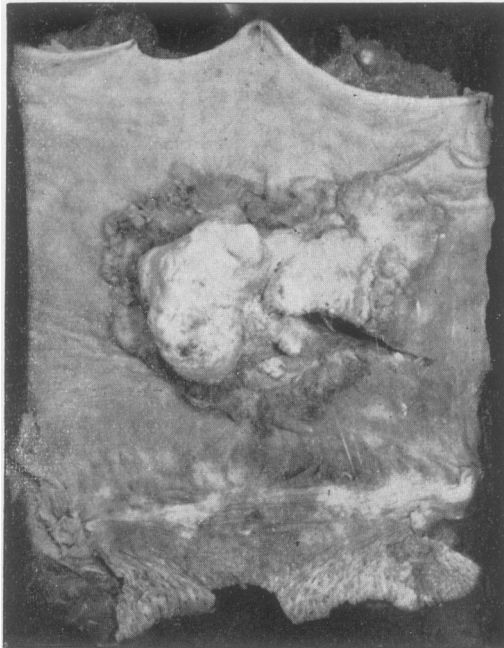


FIG. 1 (*Case 1*).—Surface view showing ossified area in the centre of malignant ulcer.

but those from the central projecting portion showed extensive areas of necrosis in the stroma and innumerable spicules of bone. Not having seen anything like this before, I took the sections to Dr. G. W. Nicholson, who had previously reported a case of ossification in an epithelioma of the skin. He kindly examined the sections and agreed that this was an example of ossification within connective tissue. The patient made a good recovery from the operation but died abroad four years later at the age of 73.

*Case 2.*—The patient was a woman, aged 32, under the care of Mr. Naunton Morgan. She had complained of rectal symptoms for several months. Sigmoidoscopy revealed a tumour in the upper third of the rectum and this was removed by abdomino-perineal excision on March 23, 1939.

The growth was ulcerating in character and measured about 2 in. in diameter. The central portion of the ulcer was occupied by a large dark projecting tumour (fig. 2). When this was incised a grating sound was noticed and spicules of bone could be felt on the cut surface. Microscopic examination showed the tumour to be an adenocarcinoma, very well differentiated in character and obviously of a low grade of malignancy. In most parts the growth had the characters of a Grade I tumour, but at the edge the arrangement was rather more irregular, so it was finally classified as Grade II (Broders). Numerous necrotic areas were found in the stroma of the projecting

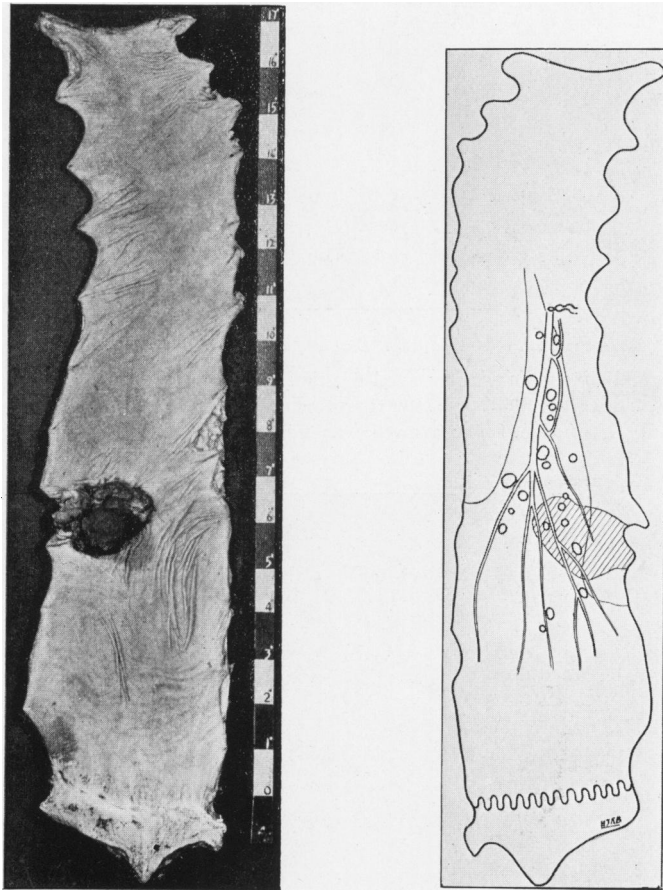


FIG. 2 (Case 2).—Surface view of rectal tumour and photograph of gland dissection.

portion of the growth and several spicules of bone were found in each of the sections (fig. 3). The growth had spread into the rectal muscle but there was no sign of spread in the perirectal fat. There was no evidence of venous spread and the lymphatic glands were all free from metastases. The growth was classified as an A case. The patient made a good recovery from the operation and is still in good health. Three weeks after the operation chemical analysis of the blood showed both the serum calcium and plasma phosphorus to be normal (10.9 and 2.0 mgm. respectively).



FIG. 3 (*Case 2*).—Section through stroma of tumour showing spicules of bone.  $\times 130$ .

*Case 3*.—The patient was a woman aged 63, under the care of Mr. A. O. Gray, who in the course of a laparotomy (14.4.39) discovered the presence of a tumour of the pelvic colon which he removed by Paul's operation. The growth was very constricting in character and dense in consistence (fig. 4). The cut surface showed several circumscribed yellowish-white areas and a

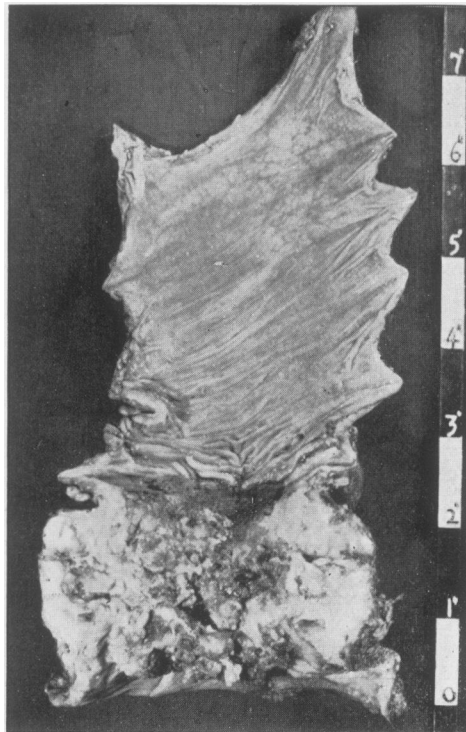


FIG. 4 (*Case 3*).—Surface view of growth.

grating sensation was noticed on scraping the surface with a knife (fig. 5). Microscopic examination showed the growth to be an adenocarcinoma, very well differentiated in type and of a low grade of malignancy (Grade I). Deposits of mucoid material and areas of necrosis were found in the

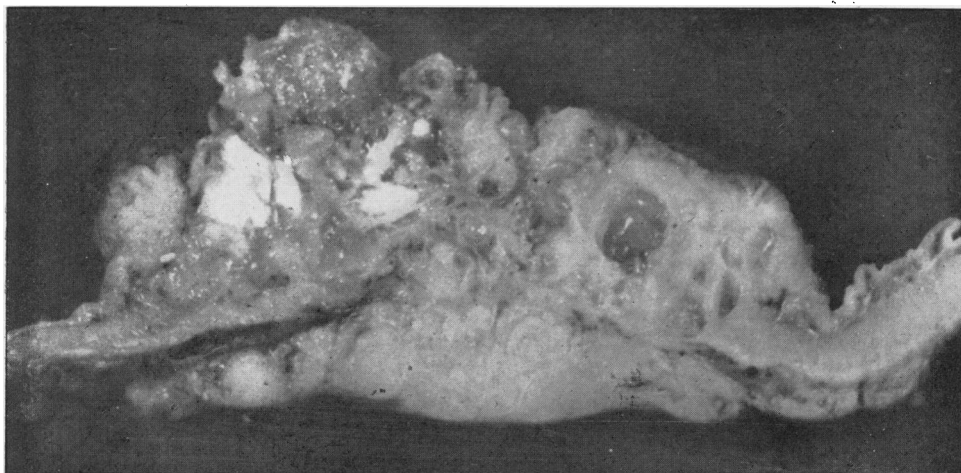


FIG. 5 (Case 3).—Slice through growth (enlarged). Centres of ossification are white in appearance.

stroma and a few spicules of bone. There was slight extension to the pericolic fat, no sign of venous spread, and the lymphatic glands were all free from metastases. The patient made a good recovery from the operation.

*Case 4.*—The fourth case differs in that the ossification was found not in the primary tumour itself but in a recurrence situated between the rectum and sacrum. The patient was a man aged 53, under the care of Sir Charles Gordon-Watson. He was first admitted to St. Mark's Hospital in October 1922, when a small adenoma was removed by the operation of posterior proctotomy. Although microscopic examination did not reveal any malignancy, it seems certain from the patient's history that a small focus of carcinoma must have been present because the tumour recurred and formed a large mass between the rectum and sacrum. At first this was thought to be an abscess, but tissue removed for section showed malignant growth, so the whole recurrence was excised in March 1927, four and a half years after the first operation. The recurrence consisted of a huge kidney-shaped tumour which was very hard in consistence but could be cut with a knife. It was surrounded by a dense fibrous capsule which was attached to the sacrum, sacro-sciatic ligament, and gluteus maximus muscle. Fragments of bone could be seen and felt on the cut surface. Microscopic examination showed the growth to be an adenocarcinoma of a very low grade of malignancy (Grade I). Spicules of bone were scattered throughout and there were several areas of necrosis. The history of this case has already been published (Dukes, Morgan, and Gordon-Watson 1928), and the only fact to add is that the patient died in March 1929. The case differs from the other two in that the bone-forming tissue may have been derived from the sacrum or coccyx and may not actually have been present in the primary growth. None the less it resembles the other two in the following particulars. The growth was of a very low grade of malignancy and continued for four and a half years without undermining the patient's health or extending to any other part of the body. As in the other two cases also, areas of necrosis were present in close proximity to the foci of classification.

Pathological ossification occurs in a generalized form in the disease *myositis ossificans progressiva*, in which there is a congenital tendency to formation of bone within the connective tissue between muscle fibres. Ossification occurs in muscles in a localized form also, usually as a result of irritation and contusion, as in the development of bone in the adductor muscles of riders and in the deltoid of soldiers,

due to the shock of rifle firing. Perhaps the most frequent site of heteroplastic bone formation is in sclerotic arteries and within calcified foci in the lungs. In these situations ossification occurs in comparatively avascular areas where metabolism is at a low ebb, and it is as a rule associated with necrosis and calcification. Jones and Roberts (1934) consider that the calcification which occurs in avascular tubercular lesions, in costal cartilages, and in the fibrous walls of blood-vessels, is due to lowered metabolism assisted by the fibrosis which follows trauma and injury.

Pathological ossification is usually the result of metaplasia, the cells of fibrous tissue becoming changed in their morphology and function so that they now form bone. In considering how this change can be brought about it is important to remember the influence that one type of cell exerts in another. For instance, Huggins (1931) has shown that the epithelium of the upper urinary tract provokes osteogenesis when implanted into the abdominal wall of dogs or rabbits. He made transplants of epithelium from the bladder, ureter, and renal pelvis, into the rectus sheath, fascia lata, and subcutaneous tissue of the abdominal wall, and found that true spongy bone with Haversian canals containing fibrous and hæmopoietic bone-marrow developed round these transplants. The stimulus to osteogenesis seems to be provided by proliferating epithelium, so that metaplasia to bone-forming tissue may be attributed to the influence of certain types of epithelium on connective tissue. Most examples of metaplasia with which we are familiar appear to serve some useful purpose. For instance, the metaplasia of the epithelium of the renal pelvis which occurs in association with calculous disease gives rise to a more resistant type of epithelium, namely squamous. If there is any advantage in the ossification which occurs in connexion with transplants of urinary epithelium, or in the ossification of rectal cancer, then all we can say is that the advantage is not obvious at present.

Although I have not been able to find any more recorded cases of ossification in rectal cancer, these four cases have some points of resemblance to the example of ossification in squamous-celled carcinoma of the skin described by Nicholson (1917). This was a tumour from the subcutaneous tissue of the pectoral region which grew very slowly, underwent necrosis, and became calcified. The necrotic areas became invaded by granulation tissue which acquired the structure and formation of marrow and deposited rings of bone round the calcified deposits. The bone was formed by direct conversion of the fibroblasts of granulation tissue into bone corpuscles.

Something of the same sort appears to have taken place in these four intestinal tumours. They were all of a low-grade of malignancy and grew exceptionally slowly, and they all contained areas of necrosis in the stroma. These facts indicate that metabolism must have been at a low level. The stationary condition of the tumour and the proximity of necrotic tissue seem to have been the factors which provoked the metaplasia of the connective tissue. Thus the connective tissue reverted to the structure which offers the strongest support and is the most resistant to decay, namely bone.

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