

viously said, are nothing more or less than tubercular tumours with fluid contents, have recovered by aseptic drainage without removal of any portion of the wall, and without any antiseptic application to their interior. For example, of 58 spinal abscesses which had been under treatment, 38, or over 65 per cent., had been cured up to the time when the statistics were made up, while others were doing well, and the list of cures would have been larger had not some of the cases become septic. Then, again, in some instances, I intentionally perform a partial arthrectomy, only removing a portion of the tubercular tissue, and in suitable cases a cure has followed. I need not take up further time by referring to other instances, such as subperiosteal excisions and excisions as ordinarily performed, where cure results, although the disease is by no means entirely removed. But even where we attempt to remove all the disease, unless we do it by amputation wide of the joint, the condition in which the wound is left is not the same as after an operation for cancer. In performing arthrectomy or excision, we cannot avoid cutting through tubercular tissues, and there is no doubt that after the operation a large amount of the tubercular virus is left in the wound, and that the wound would certainly become infected again after the operation were it not that the tissues have a great power of overcoming the parasite, so long as they are not weakened by other causes, such as septicity. These facts are sufficient to show that the analogy with cancer is a bad one, although I think that those who take the view of great curability and persist in expectant treatment in all cases are also wrong, for no doubt, in many instances, the cure can be much expedited and the ultimate result improved by suitable operative measures.

The other question, that of the risk of dissemination of the tubercular virus in cases of joint disease, is a very difficult one; and I can only express in a few words the conclusions at which I have myself arrived. That patients the subjects of tubercular joint disease often become affected with tubercular affections elsewhere, especially phthisis and tubercular meningitis, is of course well known. The question which bears upon treatment is how far these tubercular lesions are due to direct infection from the affected joint and how far they arise independently. As has been pointed out, more especially by König and Volkmann, the occurrence of tuberculosis in other parts of the body subsequently to disease of a joint does not necessarily imply that infection has spread from the joint first affected. Thus, in the first place, the infection of the various organs or parts of the body may occur at the same time, the virus being carried from some common source and deposited in the various parts simultaneously; secondly, the virus may be distributed from the original source, such as a bronchial gland on various successive occasions; thirdly, subsequent development of the disease may be due to fresh infection from without, quite independently of the primary deposit; and, fourthly, it may be the result of direct infection from the primary bone and joint disease. It is thus obvious that even complete removal of the joint trouble by amputation does not by any means guarantee the patient against an outbreak of tubercular disease elsewhere, and the only question, therefore, is as to the degree of danger involved in the presence of these local deposits and as to the amount of protection obtained from their removal.

As regards acute tuberculosis, there can, I think, be little doubt that in some cases the source of the general infection is the diseased joint. In the case of hip-joint disease in which acute tuberculosis is most common, the proportion of cases is something like 4 per cent. Now, though one of these cases might possibly be rescued by early operation, there is no doubt that in some instances the operation itself is, directly or indirectly, the cause of the dissemination of the virus; and as a matter of fact, the mortality from this disease after excision is still from 2 to 4 per cent. König states that of eighteen cases of acute tuberculosis in his practice, sixteen occurred after operation; and in my own statistics, I have a record of seven cases of tubercular meningitis occurring after operation, two at least being, I think, directly caused by it. My own opinion is that while it is quite possible that some cases might not occur if early operation were performed, this advantage is counterbalanced by the risk that the operation itself may lead to dissemination of the disease, and therefore I do not think that the hope of saving a patient from acute tuberculosis is of itself a sufficient reason for operating.

(To be concluded.)

## A CASE OF PRIMARY CARCINOMA OF THE ILEUM.

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PRIMARY CARCINOMA of the ileum apart from the ileo-cæcal valve is so rare an occurrence that I have thought it worth while to describe with some detail a case in which opportunity was afforded to make a careful examination. Among the not very numerous records of such growths I have been able to find but one paper in which a thorough microscopical examination was made—a paper by Lubarsch, in *Virchow's Archiv*, Bd. cxi., entitled, "Ueber den primären Krebs des Ileum nebst Bemerkungen über das gleichzeitig Vorkommen von Krebs und Tuberculose." The two tumours described by this author present several interesting peculiarities in common with mine; but, as will be seen later, in the interpretation of the appearances we are to some extent at variance. The subject of the growth to be here described was a patient in University College Hospital, under the care of Dr. Ringer, to whose kindness I am indebted for permission to use the notes of the case.

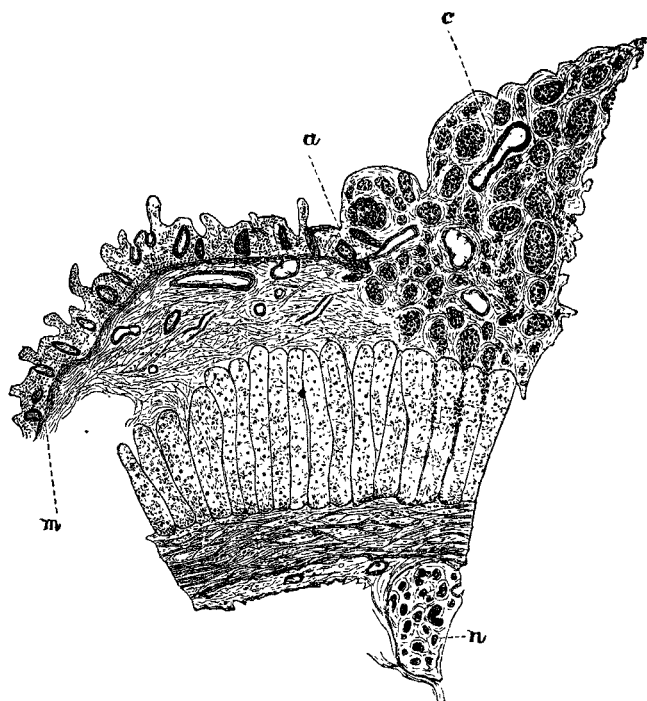
M. W—, a married woman aged fifty, was first admitted in December, 1887, suffering from metrorrhagia, and complaining also of two lumps, about the size of an egg, in the lower part of the stomach. She had also "pain after food, with diarrhoea, sometimes passing five or six stools after a bit of food." Of her previous history it was known that she had had scarlet fever as a child, and an illness called "dysentery" twelve years ago. At this time the nature of the swellings in the abdomen appears to have been not clear, the possibility of fibroids being discussed. She improved somewhat, and left the hospital in a few weeks. All through 1888 the diarrhoea continued, as well as occasional hæmorrhage from the uterus. In January, 1889, she re-entered the hospital under the care of Dr. John Williams, who removed a small polypus from the os uteri. In March, 1889, she again came under Dr. Ringer. She now showed distinct cachexia, and the abdomen seemed filled by a large hard and tender mass, the greater part of which was certainly liver. Her sufferings were further complicated by severe attacks of dyspnoea, aggravated by taking food. In April, 1889, she died.

*Necropsy.*—On the abdomen being opened it was found that the much enlarged liver nearly filled that cavity, reaching to within an inch of Poupart's ligament. The liver substance was studded throughout with numerous cancerous nodules, which varied in diameter from one-twelfth of an inch to two inches. Most of them were hard, some caseating, some hæmorrhagic. The wall of the bile-duct was infiltrated, but no primary growth of either duct or gall-bladder was discoverable. The portal glands were enlarged and cancerous. The œsophagus, stomach, cæcum, colon, rectum, pancreas, and spleen were quite free from any growth. The kidneys were granular, but free from growth, as were also the suprarenals. The bladder was normal. In the uterus some small nodules, shown to be fibroids by microscopical examination, were present on the surface of the fundus; but the organ, as well as the ovaries and vagina, was entirely free from carcinoma. The breasts were normal. Lungs emphysematous, with no growths. Heart small and fatty. On the ileum, about six inches above the ileo-cæcal valve, there was visible a small transverse puckering, on which were a couple of small nodules. The puckering was about two-thirds of an inch in length, and hardly constricted the gut. On opening the ileum, the puckering was found to be the seat of attachment of a rounded polypoid growth, which projected freely into the lumen of the gut. The growth was of the size of a small walnut, had a slightly mammillated surface, and was nowhere ulcerated. No other growths or ulcers were found in the intestines, the mucous membrane of which presented no conspicuous change to the naked eye. A vertical section through the centre of the tumour showed it to have a moderately firm consistence, and to be situated almost entirely internal to the muscular coats, which were clearly defined at the base. A few very fine white streaks, however, seemed to connect it with the small nodules on the peritoneal surface.

For the purpose of microscopical examination the material was hardened in bichromate of ammonia followed by alcohol,

and sections were made after embedding in paraffin and mounted on slides by Mayer's albumen method, so that no cells could drop out. A few sections were also cut in the usual way in frozen gum. I shall first describe the condition of the mucous membrane in the neighbourhood of the tumour, and then trace the changes to the centre of the growth. An inspection of the mucous membrane under a low power (Fig. 1) shows a distinctly abnormal condition,

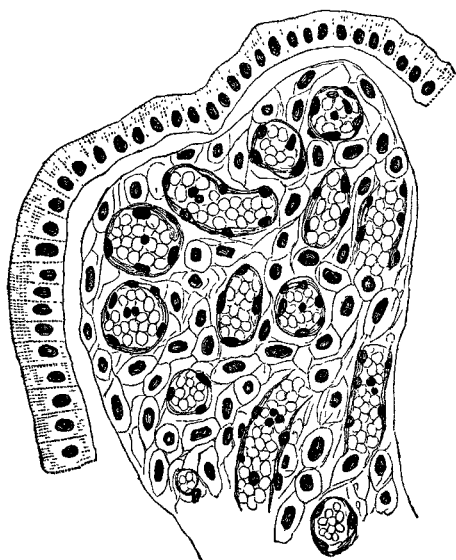
FIG. 1.



a, Edge of growth. c, Dilated crypt of Lieberkühn. m, Muscularis mucosæ. n, Nodule on serous coat.

but no sign of neoplastic activity. Even in the paraffin sections the surface epithelium is absent except in patches, the crypts of Lieberkühn are scattered irregularly and often separated by considerable tracts of connective tissue, and the villi are few, mostly shrunken, and of irregular shape. Of the central lacteal no trace as a rule remains, but the substance of the villus is made up of very vascular connective tissue, in which the capillaries are in places so abundant as to give almost an angiomatous appearance. (Fig. 2.) The scanty intercapillary tissue consists of oval and

FIG. 2.

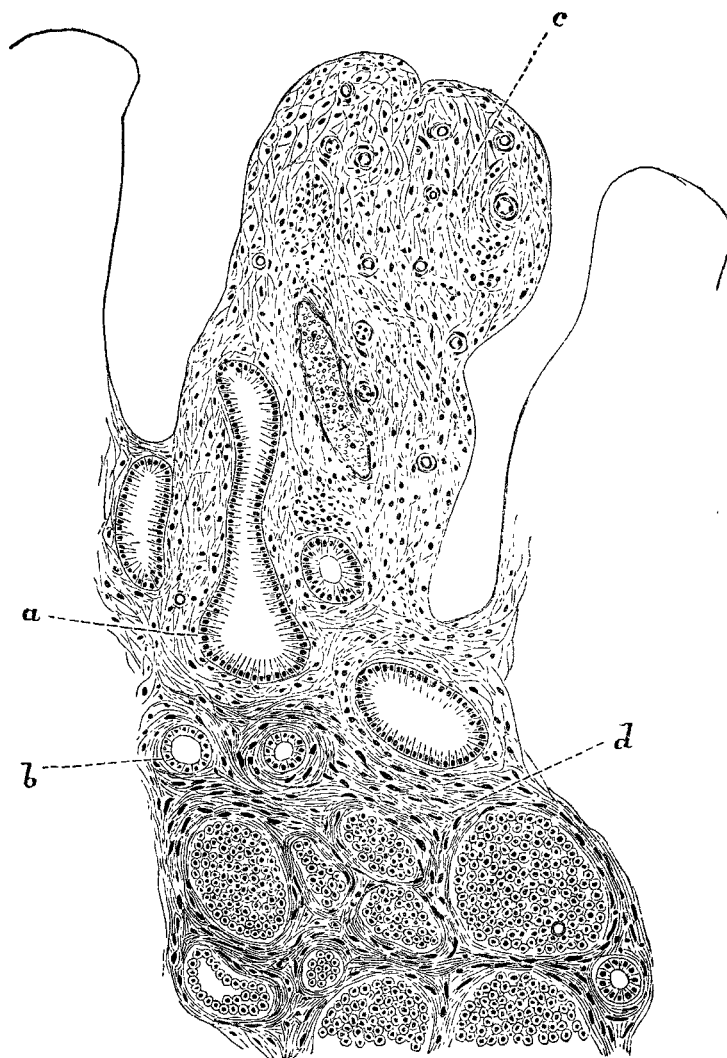


Note.—The engraver has inaccurately given the epithelium cells a striated border.

fusiform cells. The cells of the surface epithelium nowhere present a striated border, and occasionally show a tendency to change from the columnar to the cubical form. The epithelium of the crypts is fairly normal. The muscularis mucosæ, submucous, muscular, and serous coats show no changes of importance. Approaching the tumour itself, we

find at the angle formed by its projection that the crypts of Lieberkühn grow deeper, bifurcate, and present cystic enlargements, the lumen of which may or may not be traceable into that of the crypt; the epithelium of these small cysts in many cases shows no difference from that of a normal crypt, and the spaces often contain an apparently normal mucoid secretion. A few such cysts are found almost in the centre of the tumour, and these are probably discontinuous with the surface crypts. On the summit of the growth we find traces of villi, hypertrophied and consisting of a vascular connective tissue similar to that already described, and here also the crypts of Lieberkühn show similar hypertrophy and cyst formation while retaining frequently their normal epithelium (Fig. 3, a). Alongside these dilated crypts occur numerous wide tubes, in which the character of the epithelium is completely changed from columnar to cubical (Fig. 3, b). They occur in close proximity to the former; they contain a less, but similar, secretion, staining blue with hæmatoxylin, and not red with eosin, and transition forms are visible. There can

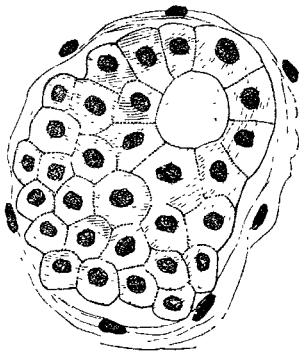
FIG. 3.



be no doubt that the slender columnar cell, with relatively small and oval nucleus of the normal crypt, has lost its inner half and become reduced to the cubical cell, with relatively much larger and rounder nucleus. But a further change yet occurs. These cubical cells may proliferate at one side of the tube (Fig. 4), and form a solid outgrowth, which may attain such dimensions that we have a large cancer acinus with an inconspicuous hole near a margin. A basement membrane is not seen round such an acinus. It may also happen, but more rarely, that the cross section of a tube exhibits tall columnar cells, hardly differing from those of a crypt, on the one side, while on the other they become shorter and squarer, and continuous with a solid mass of rounded cells forming a cancer acinus. We have thus evidence of the formation of the carcinomatous cell masses from the epithelium of the intestinal glands. In the centre of the tumour the acini form considerable masses, sometimes rounded, sometimes cylindrical, and often forming an irregular meshwork. Near the free surface of the sides of the tumour hardly any remains of villi or of

crypts of Lieberkühn are visible, and here the cells are arranged in much smaller masses, forming small tubes or solid bars, often but three or four cells thick. Stroma in this portion is practically absent, the cell masses being separated only by capillaries supported by a minimum of fine connective tissue, almost as in a normal liver. The relation of stroma to the epithelial cell masses is throughout this tumour peculiar. In those portions where dilated crypts or small cysts with normal epithelium lie in close proximity to solid acini, the stroma consists of a scanty and delicate vascular connective tissue, which presents exactly the same characters whether it lies between the crypts or the acini. The stroma of the superficial layer at the summit of the tumour (Fig. 3, *c*) is, as has been mentioned, like, though more abundant than, that of the villi of the adjacent mucous membrane. But the bulk of the stroma in the centre of the tumour is formed by the hyperplasia of the muscularis mucosæ (Fig. 3, *d*). Of the accuracy of this statement I have convinced myself by the careful study of many sections stained in various ways. A section through the margin of the growth and adjacent intestinal wall shows the muscularis mucosæ of normal size till the edge of the growth is reached. Here it opens out into a brush-like expansion, and sends numerous strands up into the centre of the tumour, and some downwards to accompany the acini into the submucous coat, so that in places its fibres almost unite with those of the circular coat of muscles. The appearance of the fibres and their nuclei are in every respect those of the smooth muscle fibres in the wall of the intestine. A similar hyperplasia of the muscularis mucosæ was noticed by Lubarsch in the second of the two cases described by him, and the growth of the smooth muscle of

FIG. 4.



the bladder to form the stroma of an epithelial tumour is described and figured by Virchow<sup>1</sup> under the heading "Myocarcinoma." The variety of the supporting tissues in the present tumour, and the total absence of anything that can be considered a new or specific stroma tissue, point to the secondary importance of the stroma of carcinomata, and lead to the conclusion that what impresses us so strongly in contemplating a scirrhous of the breast is not a primary and essential part of the tumour, but the result of a secondary and possibly reactive process. The carcinoma, in short, belongs to the histioid rather than to the organoid group of tumours. It is essentially a neoplasm of one tissue, and not of a combination of tissues. The acini, which in the present case are indisputably of epithelial origin, are the one necessary part of the carcinoma. Nor is it essential that they be arranged in alveoli; for while in typical cases there is some portion, usually the older, in which definite alveoli exist, in this primary growth and in the secondary growth in the liver, we find at the marginal and newer parts a meshwork of anastomosing rods and tubes separated only by capillaries without appreciable connective tissue. Moreover, as is well known, the outlying cells of a growth which infiltrates muscular and other tissues penetrate that tissue without accompanying stroma. The appearance of a meshwork presented by the cancer masses in the present tumour is not entirely dependent on the growth of slender rods and tubes, but is partly due to the fact that the larger acini which are in definite alveoli frequently present one or more holes in their midst. These holes, at first puzzling, are found to be of two kinds. The first is surrounded by cubical or even columnar epithelial cells, and may contain a certain amount of apparently secreted substance staining blue with

hæmatoxylin. The holes of this kind resemble those described by Friedländer<sup>2</sup> as due to hyaline degeneration of tumour cells, and Lubarsch appears to consider some of the holes observed by him as due either to hyaline or colloid degeneration. In the present case no such degeneration is observable, and the study of the smaller acini, such as Fig. 4, show that these holes are really the remnant of the gland lumen, the contents of which present the same staining reactions as the normal secretion. The second kind of hole is due to extremely delicate bloodvessels which grow into the acinus from the wall of the alveolus, and may divide so as in cross-section to produce a number of holes (Figs. 5 and 6). In most of these a very delicate wall can be distinguished; but in some of the larger ones present a perfectly circular space filled with blood-corpuscles apparently in immediate contact with healthy cancer cells (Fig. 6).

FIG. 5.

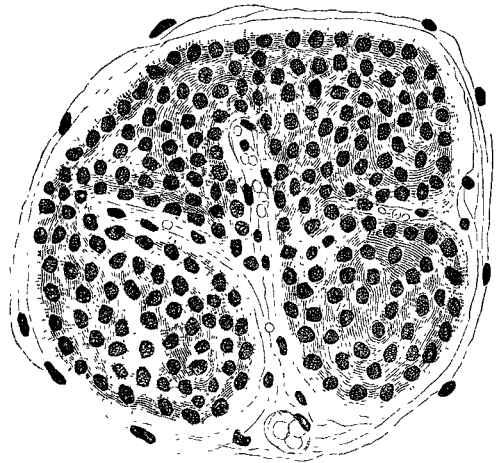
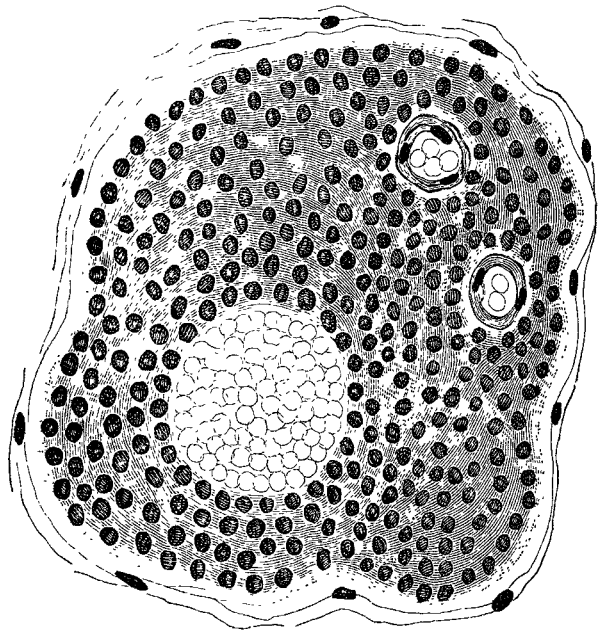


FIG. 6.



The question arises whether we are here dealing with the spread of cancer cells along perivascular lymphatics, or whether the vessels are of new formation and attendant on the epithelial proliferation. Lubarsch considered that the former view explained the meshwork appearance in his cases, and it is clear that such a mode of growth would produce such an appearance. There can, however, be little doubt that most of these capillaries are of new formation. The bulk of the new growth, the way in which the capillaries project into the large cell masses from the walls of the alveoli in parts where there is no trace of pre-existing normal tissue, and their similar relations in the secondary growths of the liver, sufficiently indicate this. They may be compared to some extent with the axial bloodvessels of the villi of papilloma of the bladder. The cancer cells are thus in the closest contact with the delicate capillary wall, and in places seem themselves to form the wall of definite sinuses.

<sup>1</sup> Die Krankhaften Geschwülste, Bd. iii., p. 121.

<sup>2</sup> Virchow's Archiv, Band lxxvii., p. 121.

This penetration of the epithelial cell masses by blood-vessels is a most unusual occurrence in carcinoma, it being often stated that such an intimate relation occurs only in sarcoma. The "villous tumour" of the bladder presents, however, a somewhat similar relation of cells to capillaries, and I have also observed it in so-called adenomata of the kidneys. It is possible that attention being directed to the point, this arrangement may be found more general. The walls of pre-existing bloodvessels are, however, in places in close contact with the cell masses, which may project and even burst into the lumen of a vein. The total absence of growth in the lymphatics of the serous coat of the intestine and in the mesenteric glands shows that the infection of the liver must have taken place entirely by the portal vein. The secondary growths in the liver reproduce nearly all the appearances of the primary tumour. The cystic Lieberkühnian glands are absent, and a distinct lumen is but seldom found, but the mesh-work of columns and the larger acini with their penetrating capillaries present no differences from the growth in the ileum. The liver cells themselves are flattened and degenerating in the neighbourhood of the growths. The enormous development of secondary growths is especially remarkable when compared with the small size, and to the naked eye innocent appearance of the polypoid growth in the ileum, and brings clearly into view the favourable condition of nutrition afforded by the liver to cells introduced from without. That the ileum itself supplies conditions much less favourable may be inferred from the rarity of primary growths in its course, and from the fact that they usually remain small and polypoid, and frequently do not give rise to secondary growths. The two tumours recorded by Lubarsch caused no secondary deposits, and Langhaus<sup>3</sup> describes a simple polyp a tumour almost exactly resembling the present. It would seem that these tumours may for long show no, and in any case very slight, local malignancy or tendency to infiltrate or destroy, but that their virulence is brought out by and largely dependent on the conditions of nutrition and resistance offered by the tissues. A tumour, in short, may be benign in one place and malign in another; one among the many facts which should cause us to hesitate in asserting a specific difference between benign and malignant tumours.

Primary carcinoma of the ileum is very rare. There is no case recorded in the Pathological Transactions, the nearest approach being a polypus described by Mr. Durham (1885) in the ileum of a girl whose colon was covered with small villous polypi. Mr. Treves, in his "Intestinal Obstruction," has collected ten cases of stricture of the small intestine due to cancer, but it is not stated in what number the growth was primary. Lubarsch after a careful search through continental and English literature finds records of thirty-five cases occurring apart from the ileo-cæcal valve, but is of opinion that several of these were not true carcinomata. Very few detailed descriptions of the form of cancer have been given, and it seems to have been assumed that columnar epithelioma is the rule. My case, the two of Lubarsch, and probably that of Langhaus, are better described as glandular carcinoma, although from the peculiar appearances produced by the penetrating bloodvessels they present some resemblance to cylindroma.

As to the conditions which favour the occurrence of primary carcinoma in the ileum, but little can be said. When Mr. Durham exhibited at the Pathological Society in 1885 the polypus of the ileum above referred to, it was suggested by Dr. Moxon that it might have arisen in connexion with the remains of Meckel's diverticulum. But that growth occurred in a girl of nineteen, who for five years had suffered from dysentery, and whose colon was covered with villous polypi. It is surely a more improbable view to attribute the polypi of the colon to the dysentery, and that of the ileum to congenital causes, than to consider both as in some manner associated with the long-standing intestinal inflammation. In the present case the clinical history points to a long-standing enteritis as probably antecedent to the tumour, and the microscopical examination shows chronic changes. In one of Lubarsch's cases the ileum contained numerous tubercular ulcers and tubercular nodules on the mucous membrane; and in his second case (also tubercular) diarrhoea had been a prominent symptom, the liver was cirrhotic, and there were six scattered small carcinomatous growths, as well as an ulcer in the ileum—

facts which point to a diffuse chronic change in the gut. A remarkable case is recorded by Waldeyer,<sup>4</sup> in which a carcinoma arose in the ileum at the spot where adhesions formed after the operation of ovariectomy; and Birch-Hirschfeld describes one arising in connexion with the adhesions of an old typhlitis.<sup>5</sup> Langhaus does not specially describe the state of the mucous membrane in the case of polypus of the ileum he records, but it is noteworthy that the cause of death was tubercle.

Finally I may allude to a case recently published by Israel,<sup>6</sup> in which a drunkard's stomach showing proliferating gastritis was the seat of two polypoid tumours—one a simple papilloma, the other a true carcinoma. He describes also a second case, that of a woman who died with all the signs of pernicious anæmia, in which a similar polypoid growth was found in the stomach. Naked-eye changes of the mucous membrane were in this case not marked, but recent advances in the pathology of pernicious anæmia make it probable that morbid changes in that membrane are usually present, and it is hardly probable that, as Israel suggests, mere loss of blood from ulceration of the tumour could cause the changes typical of the disease. He does not seem to have microscopically examined the gastric epithelium away from the growth. It is important to bear in mind that all through the alimentary canal considerable degenerative changes may occur which are not obvious to the naked eye, and the microscope must always be resorted to before the term "normal" can safely be used.

In conclusion, I would submit that while there is no evidence connecting cancer of the ileum with embryonic remains, there is a certain amount of support to a view which associates it in some way with the changes usually termed "chronic inflammation."

It may be of interest to compare with the above case of primary, a case of secondary cancer of the ileum recently recorded by Chiari.<sup>7</sup> Here there was an annular stricture twenty centimetres above the valve; but only the peritoneal and muscular coats were affected, while the mucous membrane was quite loosely attached to the growth, which had its primary seat in the gall-bladder.

## GANGRENE OF THE LEG IN TYPHOID FEVER.

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HENRIETTA R—, twelve years of age, was brought to the West London Hospital on Nov. 2nd, 1887. She had been ill four days, suffering from sore-throat, abdominal pain, and diarrhoea. During the last two nights there had been delirium. On admission, she had a coated tongue, sordes on the teeth, a temperature of 104°, and pulse of 124. Heart sounds were normal. There was some cough, and a few coarse râles on both sides of the chest. During the next three days the temperature varied between 103·7° F. in the morning and 104·5° at night, and there was frequent diarrhoea. In the daytime the patient lay on her side with legs drawn up, dull and irritable, energetically resenting attempts at examination. Throughout the night there was talkative delirium. On Nov. 6th, Mr. Webster, the house physician, who carefully watched the case, first noticed an abundant eruption of "typhoid" spots on the abdomen and back. The patient was restless and delirious, continually attempting to get out of bed. Pulse 128, dichrotic; evening temperature 105·4°. After cold sponging the temperature fell two degrees, and some sleep was procured by opium. During the next ten days respiration remained at about 42 and pulse 132. Delirium was constant, and excreta passed unconsciously. On Nov. 16th (the eighteenth day of the disease), morning remissions began to be more marked, but noisy delirium continued, and was uncontrolled by opium. Some hours' sleep, however, interrupted only for feeding, followed a dose of paraldehyde. On the 17th there was much subsultus tendinum; respiration was 44 and shallow; the pulse, which was feeble, had increased to 160, and

<sup>4</sup> Ibid., Bd. Iv. <sup>5</sup> Lehrbuch der Path. Anat., p. 918.

<sup>6</sup> Berl. Klin. Woch., No. 29, 1890.

<sup>7</sup> Centr. f. Pathologie, Bd. i., 9-10.

<sup>3</sup> Ibid., Bd. xxxviii., p. 550