

A Note on the Spread of Carcinoma by the Fallopian Tube.

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THE following is a preliminary note on two cases of dissemination of carcinoma by the Fallopian tube occurring in association with secondary growth in the ovary. The complete account will appear in the Archives of the Middlesex Hospital, Vol. xvii—9th Cancer Report.

The primary growth in each case originated in the stomach. In both instances described below there are found in the Fallopian tube, and permeating its tissues, numerous minute and discrete cancerous deposits arranged in such a manner that it is not at once easy to determine in what direction they are passing, or at what point or points they have entered the tissues.

It is believed that study of the illustrations and facts here presented reveals the fact, that cancer cells floating in the peritoneal cavity are swept into the lumen of the Fallopian tube and there coming in contact with the lining, pass through the columnar epithelium to enter the lymphatic spaces of the sub-epithelial and muscular tissues, and so pass into the mesosalpinx. This short note does not take into consideration those cases of carcinoma in which a distinct mass destroys and replaces the tissues.

So far as I can discover, this mode of spread of cancer is hitherto undescribed in medical literature.

Particulars of Cases.

CASE I. was that of a woman admitted in May, 1909, to the Chelsea Hospital for Women, under Mr. Bland-Sutton, with a mass occupying the lower abdomen, movable, with its pedicle attached to the uterus on one side and a smaller mass on the other side low in the pelvis. She presented symptoms of carcinoma of the stomach, but no tumour could be felt. A diagnosis of primary carcinoma of the stomach and secondary carcinoma of the ovary was made, and an exploratory laparotomy advised. At the operation a mass was felt occupying the stomach, but its removal was considered impracticable. Mr. Bland-Sutton confined himself to performing double ovariectomy.

The parts removed consisted of (a) one ovary the size of a

football bearing upon its upper surface an elongated and attenuated Fallopian tube. The growth of the ovary was smooth externally, and on section multi-cystic with masses of solid growth between the cyst walls. The cysts varied greatly in size, contained clear gelatinous fluid, and no intra-cystic growth. The appearances suggested secondary carcinoma grafted upon a pre-existing multi-cystic ovarian tumour. The Fallopian tube was 19 cm. in length, and, except for the thinning due to its being stretched upon the upper surface of the ovarian growth, presented to the naked eye no abnormality. Fortuitous section in the course of routine work led to the discovery of its true nature. (b) The opposite ovary, about double the normal size, was solid throughout, and showed, on histological examination, extensive secondary deposit of carcinoma. The Fallopian tube accompanying this ovary was of normal length and thickness, and on careful histological examination showed no trace of carcinoma.

CASE II. was that of a woman operated on for a tumour in the pelvis and from whom only one ovary and Fallopian tube were removed. The material and details were kindly supplied by Miss H. Chambers, Pathologist to the Royal Free Hospital, where the case was treated. At operation both ovaries were enlarged and an inoperable mass was found surrounding the duodenum. The ovary in this case was about the size of a small orange, and the Fallopian tube again suggested to the naked eye no pathological lesion.

Histology of Growths.

The character of the growth is in each case similar, the type being that of a cubical cell carcinoma (?endothelioma). There is an abundant and well-formed fibrous stroma in which occur the cubical flattened cells of the new growth. In Case i, by appropriate methods of fixation and staining, Altmann's granules were demonstrated in the cells. This is contrary to the rule for carcinoma, as shown by Dr. H. H. Beckton (*Archives Middlesex Hospital*, vol. xv—8th Cancer Report).

In Case ii a discussion having arisen as to the malignant or non-malignant nature of the ovarian growth, I suggested that microscopical examination of the apparently normal Fallopian tube would perhaps aid in the elucidation of the character of the new growth. It was upon this suggestion that this second case of spread of cancer by the Fallopian tube was discovered.

In each instance the growth in the Fallopian tube is similar to that of the ovary except that there is apparently little formation of fibrous stroma.

Method of Histological Examination.

The Fallopian tube was divided into segments of 1 cm. each. Certain portions of Case i, owing to the fact that parts of the tube

were accidentally left uncovered by preservative fluid, could not be cut. The segments were numbered, fixed in formalin, embedded in paraffin and then cut in serial sections. Certain sections of the series were taken, mounted and stained by hæmatoxylin and eosin. The sections were all cut 10μ in thickness.

Microscopical Examination of Sections.

A study of the sections under the microscope reveals the following changes as one proceeds from the fimbriated extremity towards the uterine insertion:—

Case i. In the lumen of the tube are, here and there, small detached groups of cancer cells. This is well seen (Figs. 2, 3) at a distance of 5 cm. from the free end, where five distinct and separate masses occupy the arborescent lumen. Of these masses one is attached by its extremity to the columnar epithelium, while the others are perfectly free. The cancer in the lumen appears in marked relief owing to the fact that, at this point the plical folds with their sub-epithelial stroma are healthy and free from new growth.

Before deciding upon the nature of a small mass of cells when encountered in a section including the lumen of the tube, it is necessary to trace it serially in order to determine that it is really adventitious. The detached epithelium of the tube or the tip of a villous process cut transversely might at first sight be mistaken for a group of cancer cells. The distinction is, however, not difficult owing to the more deeply staining character of the cancer cells.

The form taken by carcinoma, as it may be found free in the peritoneal cavity, has often been matter for conjecture. An examination of the accompanying figures will show small groups of cells united by a fine fibrillar stroma, in which some of the cells appear vacuolated and some show mitotic figures.

Examining now the plical folds and sub-epithelial tissues, an even more striking condition is met with (Figs. 4, 5). In this situation for a distance of 8 cm. from the ampullary extremity small masses of cancer are seen, now lying apparently free in the lymphatic spaces, now actually embedded in the tissues, or again in intimate relation to the deep surface of the columnar epithelium.

The lymphatic permeation varies considerably from segment to segment, and, although little noteworthy in the tissues of the fimbriæ, yet at a point 1 cm. along the tube and in the ampullary dilatation, the plical folds appear studded with minute masses (Fig. 4).

The fimbriæ, on the other hand, show numerous minute masses which are embedded in the tissues, and, as a rule, small near the columnar surface and larger as they pass deeper into the tissues.

In certain instances the cancer cells in relation to the deep surface of the epithelium may be traced towards a neighbouring

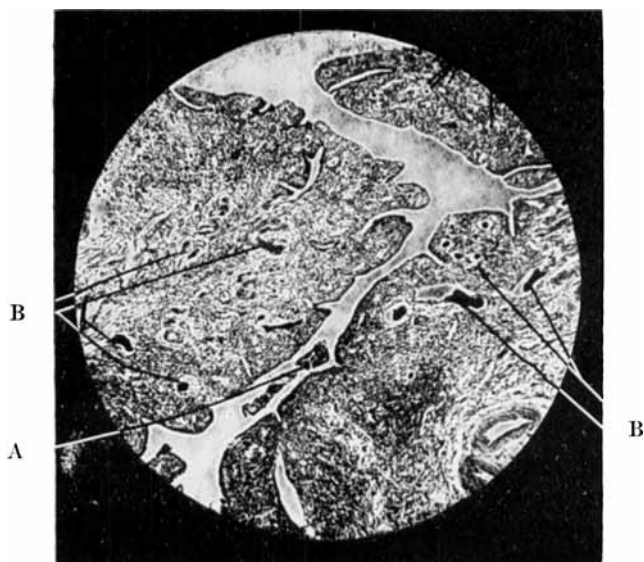


FIG. 1. Section through fimbriæ. A, masses of cancer cells free in peritoneal cavity. B, cancer in sub-epithelial tissues and lymphatics.

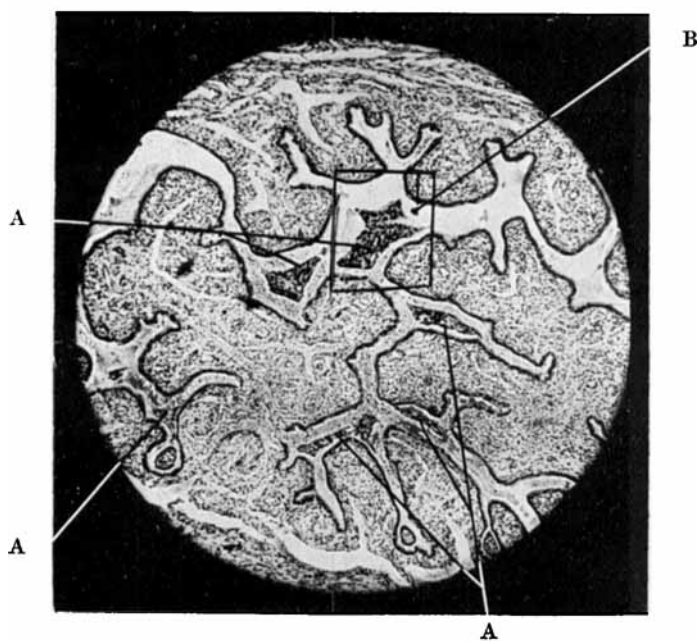


FIG. 2 (Case i). Section 5 cms. from free end. A, masses of cancer cells free in lumen; sub-epithelial tissues free from deposit,



FIG. 3. Higher magnification of B in Fig. 2. Showing tips of villous processes and a mass of cancer cells.

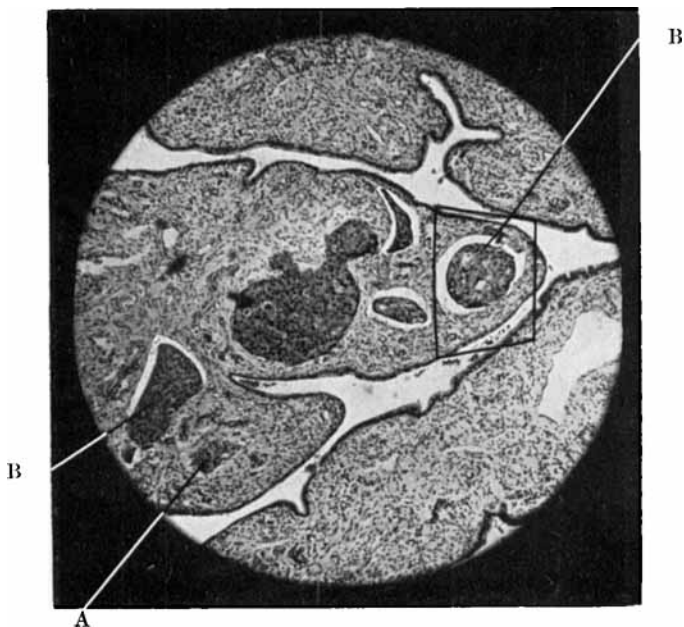


FIG. 4 (Case i). Section 4 cms. from fimbriated end. Shows villous process with deposit of cancer in sub-epithelial tissues A and lymphatics B.

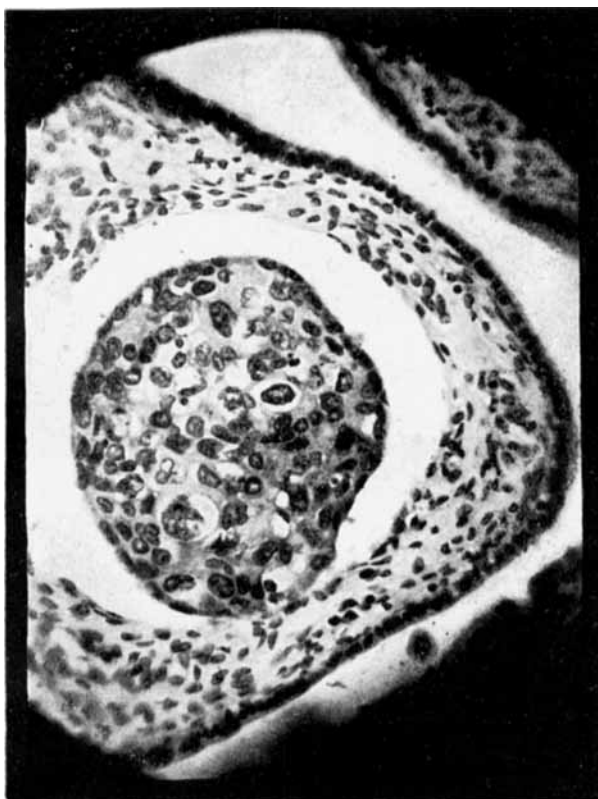


FIG. 5. Higher magnification of tip of villus in Fig. 4. Showing cancer in a lymph channel.

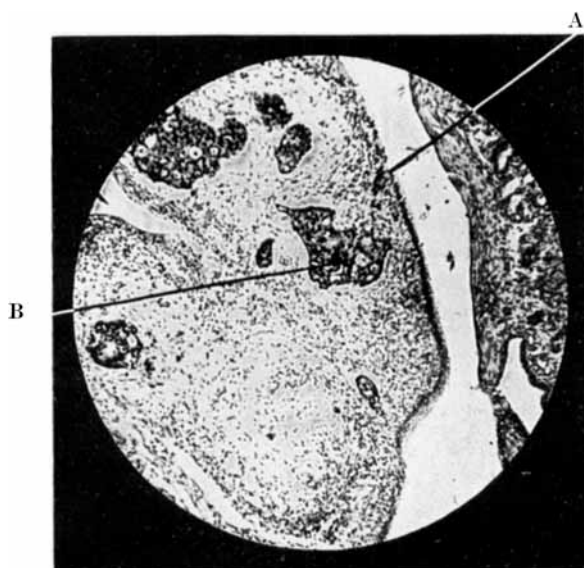


FIG. 6. Section through ampulla. At A a few cancer cells have passed through the columnar lining and lie subjacent to the epithelium.

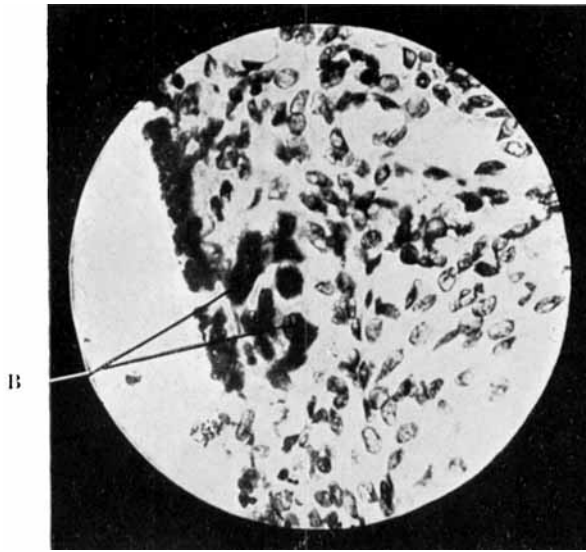


FIG. 7. Taken 10μ nearer uterine end and under higher magnification. Shows cancer cells A in sub-epithelial tissues.

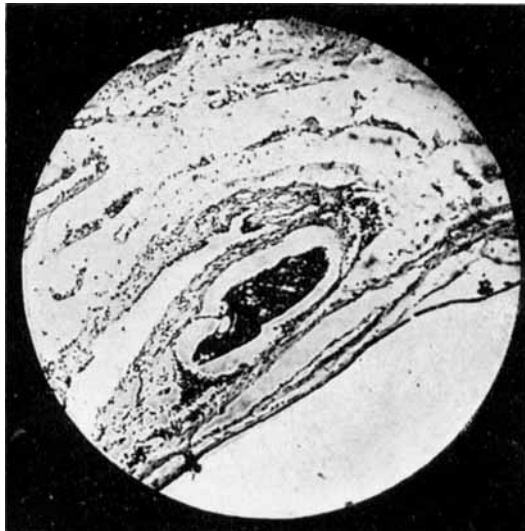


FIG. 8. 10μ nearer uterus than Fig. 7. Cancer cells A now formed into group and going to join with mass at B in Figs. 6 and 8.

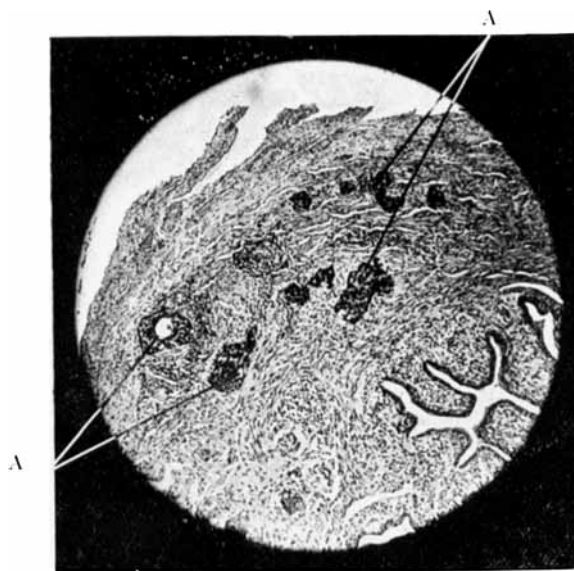


FIG. 9 (Case i). Sections 5.5 cms from fimbriated end. Shows cancer in muscular coat A.

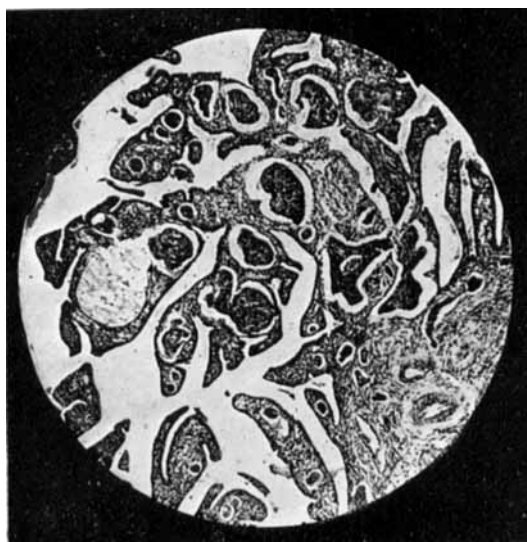


FIG. 10 (Case i). Cancerous mass occupying lymphatic efferent of mesosalpinx.

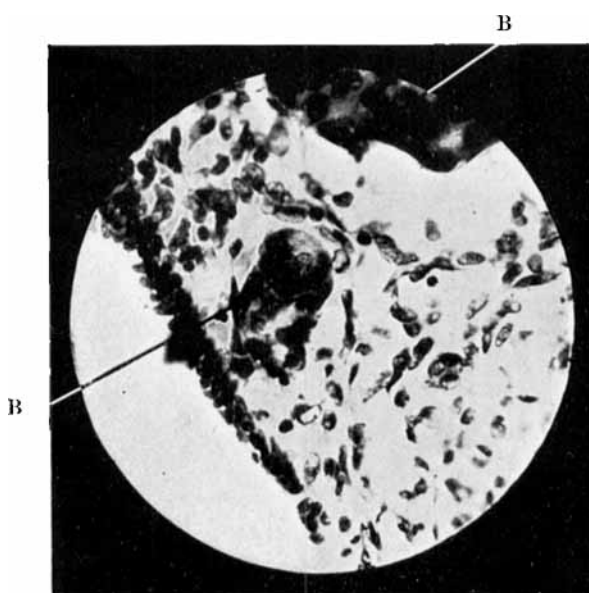


FIG. 11 (Case ii). Transverse section, showing plical folds studded with innumerable little masses of cancer.

mass of cancer occupying a lymphatic vessel. This is well shown in one series of three sections passing through the ostium of the tube (Figs. 6, 7, 8, A). In the outermost, under a low magnification the cells may be seen immediately subjacent to the columnar epithelium. In the succeeding section, *i.e.*, 10 μ nearer the uterine end, these cells become more distinctly grouped, and in a third section they have formed into a distinct mass leaving the surface and going to fuse with a mass, now but little distant, situated in a lymph vessel.

When the muscular coats are examined their comparative freedom from invasion by the spreading cancer is remarkable. Only at rare intervals may small masses be observed among the muscular fibres (Fig. 9).

In the mesosalpinx (Fig. 10), here and there, small masses of cancer occupy lymphatic channels. The total amount of growth seems, as in the case of the muscular coats, in marked disproportion to that found in the sub-epithelial tissues.

In no case could the cancer permeating the lymphatics be traced directly down to the hilum of the ovary. Invariably after following the growth through a certain number of sections it either ceased, or was found to enter larger lymphatic channels and turn outwards, as it entered the broad ligament, to accompany the main arteries.

To resume: in Case i there are found (1) free cancer in the lumen of the Fallopian tube; (2) extensive permeation of the sub-epithelial tissues and the plical folds associated with (3) comparatively little invasion of the muscular wall and of the mesosalpinx, and (4) the amount of growth and the number of discrete nodules are greatest at the ampullary extremity and in the fimbriæ and decrease as one proceeds towards the uterus.

Case ii. Here the processes are in a slightly more advanced state than in Case i, inasmuch as no part of the specimen is devoid of growth.

The growth extends as far as the point of section of the appendage from the uterus, but diminishes in amount as it nears its insertion. The plical folds show more extensive deposit, which in a few instances, is sufficient to cause destruction of the columnar epithelium and the sub-epithelial tissues (Fig. 11). Throughout the whole length there is observed slight permeation of the muscular lymphatic channels.

In the lumen small masses of cancer are found in every segment. In sections passing through the free end of the tube, and therefore cutting across the fimbriæ as they float in the abdominal cavity (Fig. 1), small free masses of cancer are encountered lying between two opposing columnar surfaces of the fimbriæ. Elsewhere in the same sections cancer cells may be seen immediately adjacent to the epithelium, and if traced serially are found to form into a small mass which eventually enters a lymphatic vessel.

In this case also the growth may be noted permeating the lymphatics to the efferent vessels accompanying the arteries of the broad ligament.

Mode of Invasion.

From a consideration of the foregoing facts it will be obvious that the cancer may have entered the coats of the Fallopian tube in one of four ways:—

- (1) Through the endothelial covering of the external surface.
- (2) Through the blood stream.
- (3) Through the lymphatic vessels.
- (4) Through the columnar epithelium lining the interior of the tube.

First hypothesis. Through the Endothelial Surface.

The small amount of cancerous growth noted in this situation and the total absence of any distinct mass replacing the normal tissues such as is encountered in secondary deposits upon a peritoneal surface elsewhere are against this hypothesis. Occasionally a lymphatic plugged with growth is encountered just under the peritoneum, but this is exceptional.

Further, in Case ii, where there is constantly found (especially upon the upper or anti-mesosalpingeal surface of the tube) a certain small deposit in the muscle, the peritoneal surface shows no nodules or irregularities, but, on the contrary, is quite normal.

Second Hypothesis. Through the Blood-stream.

Little can be said in favour of this method of dissemination in these cases. In no instance has the growth been actually seen in the interior of an artery or vein. At most a blood-vessel in a villus is seen entirely surrounded by cancer which occupies the peri-vascular lymphatics, but never actually penetrates the wall.

Third Hypothesis. Through the Lymphatics.

The course taken on this assumption would be from the ovary by the efferent lymphatic vessels of the broad ligament, and there turning off into the efferents of the Fallopian tube, it would pass back through these to the coats of that organ.

In favour of this means of invasion it is to be noted that, in each case, there is an accompanying enlargement of the ovary due to carcinoma, and that, in each case, the efferent lymphatics of the ovary show permeation by the new growth; consequently extension back into the Fallopian tube is not, *a priori*, impossible.

On the other hand, against such a manner of spread, must be considered the facts—(1) that while ovarian growths histologically similar frequently show extension into efferent lymphatic vessels, yet I have never found them to extend back into the mesosalpinx

and tissues of the Fallopian tube; (2) that in Case i, where both ovaries are enlarged, only one Fallopian tube shows presence of cancerous deposit; and (3) that the amount of growth present in the mesosalpinx in these cases is remarkably small when compared to the amount in the inner wall of the tube.

The only occasion in which invasion of the tube by way of the lymphatics may be inferred, is where the lower ovarian fimbriæ have been found adherent to the ovarian surface, and in consequence direct extension of growth has followed.

Fourth Hypothesis. Through the Columnar Epithelium.

The presence of free masses of cancer both in the lumen, and in the peritoneal cavity floating between the fimbriæ, and the large preponderance of growth in the villi and sub-epithelial tissues combine to predispose to the view that cancer cells may pass through the surface of the epithelium and implant themselves in the subjacent structures.

On the other hand, regarded from the opposite point of view, the same sections equally well demonstrate the passage of cancer cells from the sub-epithelial peritoneal tissues into the lumen.

In this respect it is interesting to note that throughout the peritoneal cavity there are but two structures devoid of an endothelial covering. One is the ovary and the frequency with which secondary carcinoma is met with in this organ is suggestive in this connection. The second structure uncovered by endothelium is the columnar surface of the fimbriæ. The above cases tend to demonstrate that the growth of cancer upon this surface is probably not infrequent.

Conclusion.

To conclude, histological examination points to the view that invasion of the Fallopian tube in carcinoma is brought about by cancer cells, which, coming in contact with the fimbriæ or being swept into the lumen, engraft themselves upon the columnar cells and thence travel to deeper parts. At present, however, one cannot entirely exclude the possibility of lymphatic permeation from the ovarian growths.