EXPLANATION OF PLATE XX.

FIG. 1.—Cylindrical-cell carcinoma of rectum, showing the invasion of the submucous tissue and muscular coat. × 20.

FIG. 2.—Section of epithelial carcinoma of tongue, showing the invasion of the muscle by long thin processes of carcinoma cells. The muscular fibres are cut transversely and show various degrees of atrophy. × 150.

FIG. 3.—Extension of carcinoma by implantation. Section of a nodule on the surface of the peritoneum secondary to carcinoma of the ovary. The tumor growing on the surface has formed vascular connections with the peritoneum, but has not penetrated the tissue. × 50.

FIG. 4.—Section through a small carcinoma of the breast, showing the rapid peripheral extension and the central atrophy. The darker areas show the places where the cells are most abundant. × 10.

Fig. 3.

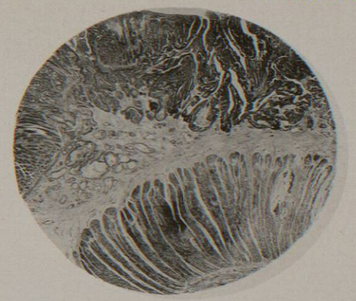

Fig. 1.

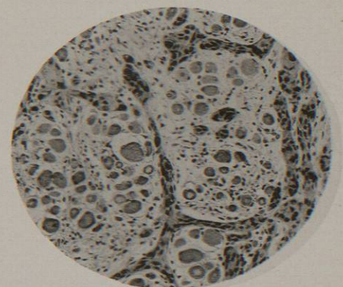

Fig. 2

Fig. 4.

PHOTOMICROGRAPHS SHOWING SOME OF THE CHARACTERISTICS OF CARCINOMA.
(COUNCILMAN.)

FIG. 1126.—Large Epithelial Pearl from Carcinoma of Tongue. The section was stained with iron hæmatoxylin which colors the keratin an intense black. (8 mm. Zeiss.)

contained in the stroma. In a carcinoma of the skin the stroma contains sweat glands, and in the mamma atrophic glandular tissue. It also contains nerves and blood-vessels. We may partly explain the new formation of stroma as a formation of tissue to carry new blood-vessels to the masses of epithelium which demand nutrition, just as the interstitial tissue is formed in a developing gland. In part, it is due to the presence of the epithelial cell masses acting as foreign bodies. In some cases it contains large numbers of cells, in others but few are present. The most numerous cells in it are small round cells corresponding to the lymphoid cells of the blood and of the lymph nodes. These are found both as a general infiltration of the tissue and in small circumscribed masses somewhat resembling lymph nodules. These cells are usually found in the greatest numbers in the periphery of the tumor, and may even form a compact mass into which the tumor grows. Next to these cells, the plasma cells are most numerous, and are more generally present in carcinomata of the skin. There are also evidences of proliferation of the connective-tissue cells, but these are not present in very great numbers and are concealed by the infiltrating cells. In a carcinoma of the uterus, where the cells grow out into a tissue composed of smooth muscle fibres, the stroma is formed of muscular tissue. The stroma should not be considered an integral part of the tumor, but it is only an accidental growth due to the mode of development and growth of the tumor. Although the connective-tissue cells in it are usually not very numerous, they may be so abundant that the stroma resembles the tissue of a sarcoma. Mucoid and other degenerations of the stroma are not uncommon. The relation between the stroma and the epithelial masses may be affected by the rapidity of growth of these. When the alveoli are numerous, by their constant enlargement the stroma may be reduced to mere shreds of connective tissue which lie within the cell masses, giving the tumor, or certain foci in it, the appearance of a sarcoma. In the scirrhous type the stroma changes its character, becoming converted into a tissue similar to cicatricial tissue. In this the cells are very few, the fibres are fused together and hyaline. Giant cells are sometimes found in the stroma. Their formation here is analogous to their formation around foreign bodies, and is a point in favor of considering the stroma a growth excited by the epithelial cells acting as foreign bodies. They are found especially in carcinoma of the skin, in the vicinity of large epithelial pearls which sometimes occupy almost the entire alveolus, and the giant cells often contain the single scales of horny epithelium. Numbers of large epithelioid cells may be found in the vicinity of the giant cells, the group somewhat resembling a miliary tubercle.

The growth of the carcinoma as a whole is analogous to that of a single alveolus. This can be best studied in sections which are made through small tumors (Plate XX., Fig. 1). The most active growth is found in the periphery. The alveoli here are round or oblong, numerous, and the cells show but little degeneration. In the centre the alveoli are very small and angular, the cells are small and degenerated, and there are but few nuclear figures. In places the alveoli have disappeared altogether, and there is a dense hyaline cicatricial tissue and a depression is formed corresponding to the atrophic centre. The atrophy of the centre is partly to be explained by the compression and occlusion of the blood-vessels by growing epithelial masses between which they must pass, and

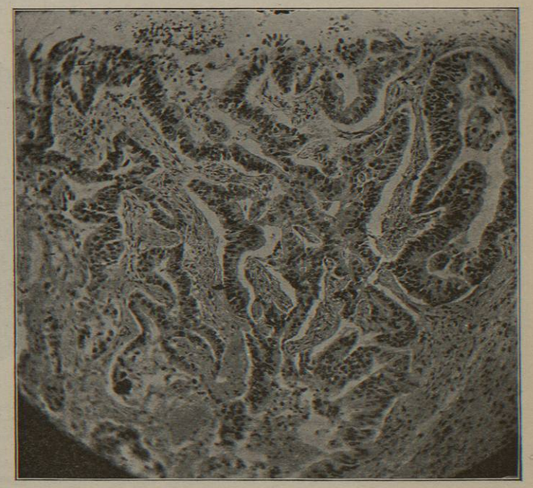

FIG. 1127.—Section of Carcinoma of Stomach. The cells have a general cylindrical type and are arranged around the walls of the spaces. (8 mm. Zeiss.)

partly by the active peripheral growth consuming the nutriment. The centre of the tumor often shows the most typical scirrhous character, while the periphery has the medullary type.

The boundary of the tumor is never sharp (Plate XX., Fig. 1); it extends in lines into the surrounding tissues.

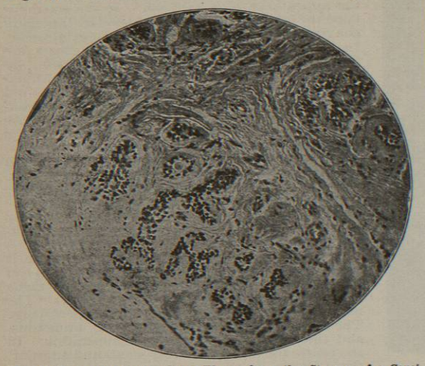

FIG. 1128.—Atrophic Glandular Tissue from the Stroma of a Carcinoma of the Mamma. (8 mm. Zeiss.)

Small masses are found in the vicinity either separated from or connected with the main tumor by a thin line of tissue. There is never any formation of a capsule, and from the nature of the tumor—a mass of epithelium growing into the lymph spaces and lymphatics—it is impossible that there should be a capsule formation. The advancing cell masses are often surrounded by infiltrating cells, but they may be found in tissue perfectly normal. Growing as it does, the tumor enters into a tissue, and the essential constituents of the tissue give way before it. The destruction and invasion of tissue in contact with it is one of the most marked characteristics of the carcinoma. The destruction of the tissue does not seem to be brought about by the pressure exerted by the growing cells, nor do the invading cells remove it by phagocytosis. This process can best be studied in the skin and in muscle. When the tumor extends toward the skin this usually becomes thin and atrophic before coming into actual contact with the cell masses. The cell layers diminish in thickness until there may be but a series of two or three cells below the horny layer. No nuclear figures are seen in the cells. Occasionally in a few places single carcinoma cells and even single groups of them may be found within the cells of the epidermis. The skin over the tumor is not elevated, but more generally depressed. The atrophy of the skin is due to the demands for nutrition made by the advancing tumor. No new cells are formed, and the old cells gradually become horny and are cast off. Where the tumor enters into the dense connective tissue of the skin there is usually a peculiar relation of cells and stroma. The small lymph spaces of the skin here cannot dilate under the pressure of the cells infiltrating it, so that there is an interlacing system of small alveoli filled with epithelial cells lying in a dense unchanged stroma. There is usually no appearance suggestive of new formation of stroma. In contact with the muscle, as where a carcinoma of the breast comes in contact with the pectoralis major, the tumor extends first along the connective-tissue septa and coarsely infiltrates the muscle. In places the growth is more rapid and small nodules may be formed in addition to the general infiltration. At this stage the muscular fibres are small and atrophic. Later there is extension between the fibres themselves. The fibres lose their striation and are converted into hyalin. In places the degenerative increase in the nuclei is prominent. Phagocytic giant cells may be formed in the stroma and these take part in the absorption of the necrotic fibres. The epithelial cells may push their way into the sarcolemma and extend within this. A section through such a place shows a general infiltration of epithelial cells arranged with some regularity in long lines parallel to the muscular fibres, and among them, small, generally angular remains of the fibres may be seen. The epithelial cells infiltrate the loose tissue, and there is no sharp distinction between cells and stroma. The same process of atrophy and gradual disappearance of tissue is seen in the extension of the tumor into such a parenchymatous organ as the liver. There is more evidence of the effect of pressure here than elsewhere. The liver cells in the vicinity are usually flattened or have a cylindrical form. In some cases, especially where the extension is very rapid, there is but little evidence of pressure even here. When the tumor comes in contact with the fat it extends in the larger connective-tissue septa, then along the fine septa between the fat cells. These become reduced to small spaces which finally disappear, the cells of the tumor filling the entire tissue. There is but little stroma in the tissue. Nothing shows better how little part the stroma plays in the tumor than the study of the periphery of a rapidly growing tumor. The abundance of the stroma has a direct relation to the amount of connective tissue in the tissue invaded. Different tumors vary enormously in the degree of their infiltration. One occasionally sees tumors in which the growth is almost as homogeneous as is that of a benign tumor, in which it is almost possible to determine the limit of the growth by the naked eye. As the direct opposite to these are tumors with such extensive infiltration that small extensions may be found far beyond what appears to be the periphery.

Not only is there this general growth by infiltration but small nodules of the tumor are found in the surrounding tissue, this being termed dissemination. These small nodules may be connected with the main mass by small lines not visible to the unaided eye, or they may be independent. They are found in carcinoma of the breast,

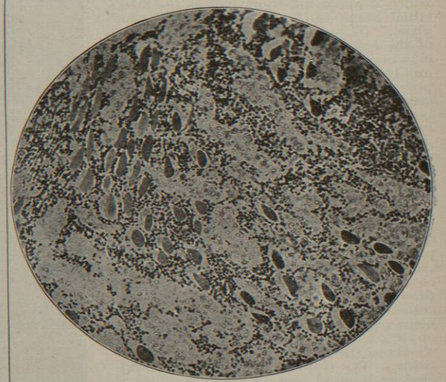

FIG. 1129.—Pectoral Muscle Invaded by Carcinoma of the Breast with great Numbers of Lymphoid Cells in the Stroma. The larger dark areas represent the atrophied muscular fibres cut obliquely. (8 mm. Zeiss.)

more generally beneath the skin than in the deeper tissue. They repeat all the characteristics of the main tumor. Their presence is easily explained by a careful examination of the tissue in the vicinity of the tumor. This often

shows dilated lymph vessels filled with small masses of epithelial cells, or, in some cases, with single cells. I have sometimes been able to see the beginning of a peripheral nodule in an extension of the epithelial growth

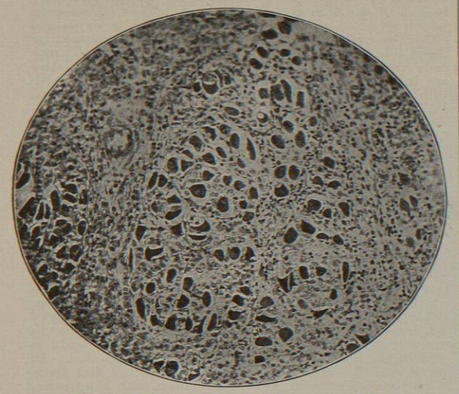

FIG. 1130.—Cross Section of Muscular Fibres Invaded by Carcinoma. The fibres are small and irregular in shape. (8 mm. Zeiss.)

from such a vessel into the surrounding tissue. The cells are carried passively in the lymph stream. Examination of the fresh tissue of a carcinoma on a warm stage shows that the cells have slight amœboid movement, limited to the extension and retraction of processes. There is no evidence of such an extent of amœboid movement as would lead to a voluntary progression of the cells into the tissue, nor is it necessary to assume such to explain these secondary nodules.

It is characteristic of the tumor not only to grow by infiltration and dissemination, but small tumors similar to the original are formed in distant parts. These are termed metastases. They are due to the conveyance of tumor cells, by means of lymphatic and blood-vessels, from the primary tumor and their deposit in the places where the metastases appear. The relation between the epithelial masses and the lymphatics is so close in the carcinoma that the metastases appear first in those lymph nodes into which the lymphatics of the tissue in which the primary tumor is seated enter. Thus in carcinoma of the breast the first metastases are in the axillary lymph nodes, in carcinoma of the uterus, in the post-mesenteric lymph nodes, etc.

We have already spoken of the fact that single tumor cells and small connected masses of them may be found in lymph vessels in the vicinity of the primary tumor.

The affected lymph nodes are enlarged and may contain small, grayish masses or be entirely converted into tumor. They may be affected and yet show to the naked eye no evidence of this. So general is this secondary affection of the lymph nodes that surgeons in all cases of operation for carcinoma of the breast remove the axillary nodes. Microscopic examination of the nodes, particularly those which to the naked eye show no lesion, often give clear indications of the manner in which the infection has taken place. The metastasis begins in the periphery of the node at the place of entrance of the afferent lymphatics. These are often dilated and contain masses of tumor cells. There may be one or a number of small tumor foci in the periphery of the node in immediate relation with the lymphatic sinuses, or these may be generally injected with tumor cells. The peripheral sinus of the node is not infrequently seen filled with growing masses of the tumor which from here extend into the lymph nodules. Between the masses of epithelial cells there is in the beginning only the lymphoid tissue of the node. After this atrophies, its place is taken by connective tissue. The character of the original tumor is repeated in the metastases, although in general the cells of the metastatic growth show less of a physiological tendency than do those of the original tumor. In the metastases of carcinoma of the skin the tendency to pearl formation is less marked, and in those from glandular carcinomata the cells do not usually show the tendencies to physiological arrangement which may be marked in the primary tumor. The extension of a primary carcinoma into adjoining tissue may involve other sets of lymph vessels. When a carcinoma of the breast extends deeply into the tissue beneath, metastases may develop in the lymph nodes of the anterior mediastinum. Only the lymph nodes which are primarily connected with the original tumor may be affected, or the process may extend from these into adjacent nodes. The tumor growth may affect the entire node, and the cells find their way into the efferent lymphatics, or they may pass through the node by means of the lymph stream without producing a growth. In extensive metastatic formation in the axillary nodes the clavicular nodes also are usually involved. The detection, by microscopic examination, of metastases in the lymph nodes is usually easy, though in some cases the lymph sinuses are filled with large endothelial cells which have some resemblance to carcinoma cells and may be mistaken for these.

Metastasis by means of the blood circulation is less common in general than that which takes place by way of the lymphatics, although in carcinoma of the intestinal canal the former mode of disseminating the disease

FIG. 1131.—Superficial Lymphatics of Skin Dilated and Filled with Masses of Carcinoma Cells. From a carcinoma of the scrotum with numerous metastases. (No. 3 Leitz.)

is the rule. The tumor cells may enter into the blood by means of the lymph circulation, or there may be a direct growth of the primary tumor into the blood-vessels. In carcinoma of the liver a growth of the tumor into the portal and hepatic veins is so common that it