Cancer of the breast and its operative treatment / by W. Sampson Handley.

CANCER OF THE BREAST

AND ITS OPERATIVE TREATMENT

W. SAMPSON HANDLEY

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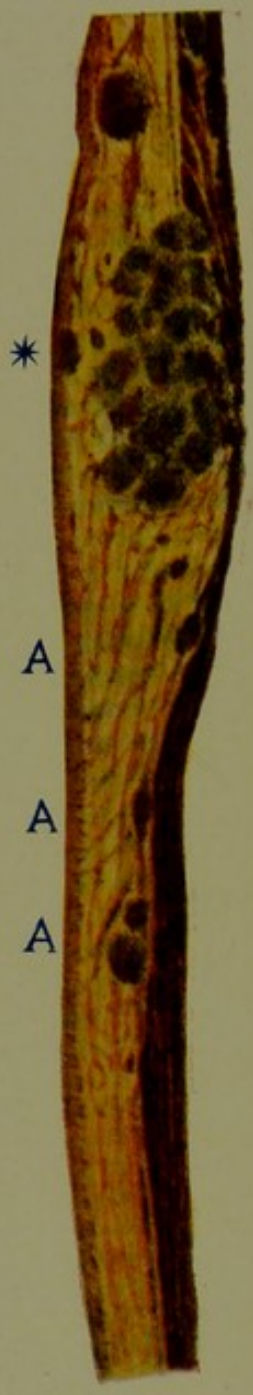
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Description of Frontispiece.

A nearly median sagittal slice, one-eighth of an inch thick, viewed by transmitted light, of the parietal tissues in the intermammary and epigastric regions from a case of breast-cancer. Natural size. The specimen is prepared and rendered translucent according to a method first described by the writer in *Archives of the Middlesex Hospital*, Vol. III. The asterisk indicates the level of the nipple. From left to right are seen the skin, subcutaneous fat, fascia, and muscle—the pectoralis major above, and the rectus in the lower part of the figure. On the anterior surface of the rectus sheath are seen cancer nodules (A A A). The skin overlying them is normal, though it shows one nodule higher up near the level of the nipple. The fascial nodules were clinically impalpable, but epigastric invasion of the abdomen had, nevertheless, occurred. In an earlier stage of this case it might probably have been prevented by the operative measures suggested in the text.

The specimen is derived from Case I., Chapter IV.

DESCRIPTION OF PHOTOMICROGRAPH.

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CANCER OF THE BREAST

AND ITS OPERATIVE TREATMENT

BY

W. SAMPSON HANDLEY

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LONDON

JOHN MURRAY

ALBEMARLE STREET

1906

To Three of my Friends:

T. H.

L. A. D.

W. H. A. J.

PREFACE.

THE following pages represent an attempt to place the Operative Treatment of Breast Cancer, hitherto in some respects still empirical, upon a more complete rational basis. They embody the results of an investigation carried out in the Cancer Research Laboratories of the Middlesex Hospital during my tenure of the "Richard Hollins" Cancer Research Scholarship, 1903-6, and partially summarized in my Hunterian Lectures for 1905. The account of parietal dissemination is based upon two papers contributed to the "Archives of the Middlesex Hospital," which are here reprinted, with additions, by kind permission of the Cancer Investigation Committee of the Middlesex Hospital. The description of visceral dissemination is largely taken from my Astley Cooper Prize Essay (1904), on "Epigastric Invasion of the Abdomen in Breast Cancer." The Astley Cooper Trustees have kindly allowed me thus to anticipate in some degree the publication of the essay elsewhere.

I have regarded questions of etiology, pathogenesis, and diagnosis as beyond the scope of this work, the aim of which is to present for the surgeon's use a careful picture of a breast cancer, of its microscopic ramifications, and of its mode of dissemination, and upon this basis to discuss the methods of operative treatment.

Though I have aimed at conciseness of statement, the subject is so complex that I have been unable, consistently with clearness and a full presentation of the evidence, to hammer my material into as small a compass as might be wished. Considerable space is devoted to the microscopical study of dissemination, for an acquaintance on the part of the surgeon with this branch of morbid histology is, in my opinion, essential to the due performance of the operation for breastcancer. The operator's eye can no more delimit the invisible margin of the growth with which he has to deal, than it can see the bacteria he aims at excluding from his wounds. In dealing with cancer, as in the practice of asepsis, he must rely upon pathology to supply him with mental pictures of the invisible—pictures for which empirical

rules are very inadequate substitutes. Upon the accuracy of these mental conceptions his operative results must to a large extent depend. Moreover, if I am right in my belief that the adoption of means to prevent epigastric invasion of the abdomen should further diminish the tale of post-operative recurrences by ten or twenty per cent., this book has for that reason alone a valid claim on the attention of all surgeons who have to deal with cancer of the breast.

The method of operation advocated in these pages has a pathological basis throughout, and is not a mere variation of technique. My aim, however, has not been the impossible one of devising a "new" operation for breast cancer, but rather to decide, by an appeal to pathology, the conflicting claims of existing methods and to embody selectively with such modifications as seemed necessary the best features of each.

I am under great obligations to those of my surgical colleagues at the Middlesex Hospital who have assisted me by detailed information as to the operative methods they employ. The account of breast-surgery given in Mr. Jacobson's "Operations of Surgery" has also been very helpful. Fig. 1 is taken from Dr. M. B. Schmidt's valuable work, "Die Verbreitungswege der Karzinome."

It is possible that the title of my book fails to indicate its full scope from a pathological point of view, and that the new conception of dissemination set forth in it—the permeation hypothesis—applies not only to cancer of the breast, but in general to most carcinomata which give rise to metastases. It will be necessary in the future to study each anatomical variety of carcinoma from this standpoint, and to revise surgical treatment in accordance with the results. Meanwhile, as the Appendix shows, I have been able to demonstrate that permeation plays a part, though a minor one, in the dissemination of melanotic growths, and that the fact has important bearings on their operative treatment.

In conclusion, I have to express my obligations for help in various ways to a number of kind friends and colleagues, and especially to Dr. W. S. Lazarus-Barlow, Director of the Middlesex Hospital Cancer Research Laboratories.

77, Wimpole Street, W.
September, 1906.

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INADEQUACY OF THE EMBOLIC THEORY OF DISSEMINATION.

Introductory.

THE subject discussed in the following pages may be tersely expressed as follows:—If a cancer of the breast is present, how ought the surgeon to deal with it? Since excision is practically the only reliable treatment at present known, the question becomes:—How can a cancer of the breast, with all its microscopic ramifications, be completely excised? The attempt to solve this problem demands precise knowledge of the paths and method of dissemination. And since a study of the evidence has compelled me to adopt a view of the process of dissemination which differs radically from that usually accepted, I must necessarily go somewhat fully into the facts and observations which justify this change of view.

All the earlier part of this book is therefore devoted to the pathological problems upon the solution of which proper surgical treatment must necessarily be based.

The Embolic Theory.

There appears to be only one current explanation of the more remote metastases in breast-cancer, such as those in the internal viscera or at distant points in the parietes—the hypothesis known as the embolic theory. In default of a rival this theory has long held its ground, but some writers, doubtful perhaps of its validity, ignore the subject of visceral dissemination entirely, or dismiss it with scant notice.

According to the embolic theory* particles derived from the primary growth obtain access to the blood, and are carried by the force of the circulation to remote districts, where their cells proliferate, and produce secondary nodules.

There can be no doubt that cancer cells frequently obtain access to the blood, either passing into it by way of the thoracic duct, or invading the small veins in the vicinity of the primary growth. Goldmann, and also Roger Williams, have drawn especial attention to the latter form of invasion. Mr. Stephen Paget† was the first to show that in its simple form, as stated above, the embolic theory is untenable. He pointed out that embolism is necessarily an impartial process, to which all the organs are liable. But the distribution of cancerous metastases in the various organs is by no means impartial. Some organs are very frequently invaded, others only rarely. Hence it is necessary to assume that certain organs form a favourable nidus for the emboli which lodge in them, while in other organs the embolised particles are destroyed or rendered incapable of growth.

In support of his view that tissue-predisposition determines the success of embolic invasion, Mr. Paget adduced some striking facts. Of 735 cases of breast-cancer, while the liver showed cancer in 241, only 17 had cancer of the spleen. On the other hand in 340 cases of pyæmia abscess of the liver occurred 66 times, and of the spleen no fewer than 39 times.

Again, since cancerous particles reaching the blood must pass through the lungs to gain the systemic circulation, it appeared remarkable that these organs showed cancer in only 70 out of 735 cases. In parenthesis it may be remarked that Zahn has explained the relative immunity of the lungs as due to the passage of cancer particles from the right to the left auricle through a patent foramen ovale (paradoxical embolism), a somewhat unconvincing explanation.

Mr. Paget further showed that each variety of primary growth has its own special metastatic geography. For

*A full statement of the embolic theory, and of its difficulties, will be found in Mr. Roger Williams' "Diseases of the Breast," 1894, p. 207; Mr. Sheild, "Diseases of the Breast," 1898, p. 455, also appears to accept the embolic theory.

†Stephen Paget, on "The Distribution of the Secondary Growths in Cancer of the Breast," *The Lancet*, March 23rd, 1889.

instance, breast-cancer as compared with other forms of carcinoma is frequently associated with fragilitas ossium, and with bone deposits. While skeletal metastases are frequent in cancer of the breast and of the thyroid, Gussenbauer and von Winiwarter found not a single instance among 903 cases of cancer of the stomach. In order to reconcile this fact with the embolic theory, Mr. Paget assumed that the tissue predisposition of the different organs varies according to the particular viscus in which the primary carcinoma originates.

Proceeding in his acute analysis of the embolic theory, Mr. Paget showed that certain bones are habitually affected in breast-cancer, while others invariably escape. In the face of this difficulty he was driven to assume that tissue predisposition to cancer is a variable factor as between different parts of the skeleton,—that while the humerus, for instance, possesses it in a high degree, the radius, equally subject *ex hypothesi* to cancerous embolism, possesses a natural immunity to carcinoma.

The embolic hypothesis, elastic though it is when interwoven with the doctrine of specific tissue predisposition, seems by such a supposition to be strained to breaking point. There can be no doubt that in certain rare cases of carcinoma, embolism by way of the blood stream does occur as a process effective in causing metastases. Such a case for example is that of R. Volk, in which a gastric carcinoma, after invading the liver, had produced cancerous pulmonary embolism. Daughter nodules were found in the kidneys, in the brain, and upon atheromatous ulcers in the thoracic aorta. But as a general explanation of metastases the embolic theory is negatived by a study of metastatic distribution. There can be no doubt that some tissues and organs form a more favourable *nidus* for cancerous epithelium than others; and Mr. Stephen Paget's clear statement of this fact must remain as a valuable contribution to the subject. But he found further suppositions necessary in order to reconcile the embolic theory with the facts of metastasis, (*a*) that the tissue predisposition of the various organs is variable and characteristic for each anatomical variety of primary growth; (*b*) that in breast-cancer tissue predisposition is present in

certain bones and absent in others; i.e. the carcinomatous emboli distributed impartially (by hypothesis) to the various segments of the skeleton are in certain bones destroyed, while in other bones they gain a footing and produce metastases. In the absence of direct evidence for either of these hypotheses, it seems to me that they are so improbable as to be inadmissible. The only claim which can be urged in their support is that, unless they be admitted, the embolic theory fails to explain many of the facts of metastasis. Such, it appears to me, is the logical and inevitable inference from the new facts adduced by Mr. Paget.

Among more recent contributions to the subject of invasion of the blood by carcinoma, the most valuable is that of M. B. Schmidt,‡ whose work has not yet received, in this country at any rate, the attention due to its importance.

M. B. Schmidt examined the condition of the lungs in 41 cases of carcinoma. Rejecting cases where the lungs were healthy, or had primarily been invaded by the lymphatics, or where the primary mode of invasion was uncertain, he obtained 15 cases showing cancerous embolism of the small pulmonary arteries. In all these cases the primary growth was situated in the abdomen.

Schmidt's cases may here be quoted in abstract:—

Case 1.—M., aet. 37. Cancer of Stomach. Metastases only in abdominal glands and in one bronchial gland. In both lungs are patches covered by numerous fine white ramifying lines, especially in the course of the vessels. The subserous lymphatics of the stomach are filled by cancerous growth, many of whose cells, especially the central ones, are necrotic.

In the lungs many of the smaller arteries, of $\frac{3}{4}$-mm. calibre or less, contain thrombi, partly fibrous, partly nucleated and hyaline. There are also mosaic-like groups of cancer cells, almost exclusively associated with the recent nuclear-hyaline thrombi, seldom included in the fibrous thrombi, occasionally free in the lumen. The older thrombi contain but few and scattered cancer cells at the most, while few of the recent thrombi are free from them. Nowhere outside the blood-vessels was there any cancer in the lung.*

Case 2.—M., aet. 37. Cancer of Stomach. Abdominal glands cancerous, not the bronchial ones (even microscopically). No other

‡ M. B. Schmidt, "Die Verbreitungswege der Karzinome," Jena, 1903.

metastases. In the parenchyma of the lungs are patches of closely set, finely ramifying white lines, following the course of the small arteries and evidently lying in their lumen. Microscopically numerous small arteries are seen filled with cancerous material. The thrombi differ in age, in the older ones the cancer cells occur mostly only in small groups, a few larger groups show a regular arrangement of their peripheral cells, in contrast to the ataxic grouping of their central cells, and are thus divisible into two layers. In places the central cells are necrotic. Here and there in the fibrous tissue are large vesicular nuclei without protoplasm, no doubt the relics of cancer cells.

The recent thrombi consist of nuclear or hyaline material enclosing large groups of cancer cells, which peripherally show mitoses, and take on stains well, while the central cells are much split up and their nuclei do not take on stains. The mass is often permeated by numerous polynuclear leucocytes, and so are formed hollow bodies, consisting of a thrombotic shell with an inner lining of vigorous cancer cells, and soft contents. In this case some of the lymph vessels also are blocked by cancer-masses whose central cells show advanced necrosis, while in the peripheral ones mitoses are visible, but Schmidt never found in the lymphatic vessels a stroma between the cancerous cells, nor any layers of thrombotic fibrous tissue around them. The boundaries of the diseased lymphatic are everywhere sharp and often the endothelial lining is quite unaltered. Sometimes the cancerous thrombus in an artery is united with cancer in a perivascular lymphatic by lines of cancer cells in the media and adventitia. But the veins in whose neighbourhood cancer-filled lymphatics are seen never show cancerous infiltration of their walls, nor thrombosis.

In a majority of the involved arteries the cancerous invasion is confined to the lumen, and involves neither the vessel wall nor the surrounding lymph-vessels.*

Case 3.—M., aet. 45. Cancer of Stomach. Abdominal glands cancerous, and one gland in the thorax. Peritoneal and sub-phrenic metastases. No others. In the lungs the small arteries of 1-mm. calibre or less are extensively the seat of cancerous thrombi, especially at their bifurcations. Most of the thrombi are of about the same age. They are fibrous and poor in cells. The cancer cells take up a great part of their area, and form gland-like or spherical spaces, similar to thyroid follicles, with a single-layered epithelial lining and mucoid contents. The lining epithelium often shows well formed goblet cells. No cancerous lymphatics are present, though the cancer in some of the arteries has penetrated to the adventitia. In the youngest thrombi the cancerous cells lie singly or in small groups.*

Case 4.—M., aet. 40. Carcinoma of Pylorus. Metastases in abdominal glands, suprarenals, left kidney, liver, thoracic gland near

the left innominate vein. All sections of the lungs show fine processes of growth, some of which are certainly in the arteries, others very near them. Microscopically arteries containing cancerous thrombi and lymph vessels filled with cancer are present extensively in the lungs. In the lymph vessels the cancer cells have no stroma, and the centre of the mass is often necrotic. In only one place was cancer seen to have broken through the wall of a lymphatic (into a bronchus).

Case 5.—M., aet. 43. Cancer of Pylorus. Metastases in the abdominal and left supra-clavicular lymph glands, and in the liver. Lungs, peritoneum, and pleura quite free from growth.

Microscopically, an extraordinary number of the small arteries and many of the capillaries and small veins of the lungs are obstructed by masses of cancer cells, vigorous, adherent to each other, and often showing mitotic figures. Nowhere round these cellular masses are there any thrombotic layers.

Case 6.—M., aet. 42. Cancer of Stomach. Metastases in retro-peritoneal glands. Small ones on the pleura of both lungs. Two cancerous thoracic glands. On section of the lungs fine white dots and lines, without lumen, were seen here and there.

Microscopically, much cancer in the lumen of the pulmonary arteries, less in the veins, least in the lymphatics, and only in the peri-arterial ones. The cancer cells are sometimes naked, sometimes surrounded by a nucleated granular thrombus. Here and there are fibrous thrombi in the arterioles, blended with their walls and enclosing small islets of scattered cancer cells. At other points are non-cancerous connective-tissue thrombi. In the veins the cancer cells form continuous strings, not enclosed in thrombotic tissue. Occasionally capillaries filled with cancer cells can be seen. Mitoses are present both in the blood and lymphatic vessels. The arrangement of the cells in two layers seen in Case 2 is not obvious.

Case 7.—F., aet. 27. Cancer of Stomach. Metastases in the abdominal, retro-sternal, left supra-clavicular, and posterior mediastinal glands. Nodules on the peritoneum, on the mucosa of the ureter, vagina, and intestines, and in the psoas muscles. Small white miliary nodules in the upper lobes of the lungs.

Microscopically, the little pulmonary nodules enclose each a small artery containing a cancerous thrombus, which never infiltrates the wall of the artery. The growth in the peri-arterial lymphatics is in places infiltrating the lung tissue.

In the rest of the lung the arterioles in large numbers are obliterated by close fibrillary tissue, in which lie nests of healthy cancer cells, without any infiltration of the arterial walls. These fibrous thrombi may be followed through the capillaries into the veins, and here also

contain cancer cells. One artery was seen with its wall perforated by growth.

Case 8.—F., aet. 76. Cancer of the Bladder. Abdominal glands cancerous, no other metastases, and especially none in the lungs.

Microscopically, in the lungs there is no cancer outside the blood-vessels, but many small arteries are filled by vascular connective-tissue thrombi, in which sometimes there is no foreign inclusion, sometimes one or more large cancer cells. Some arteries contain fresh granular thrombi, enclosing groups of vigorous cancer-cells; in others the obstruction consists of cancer-cells only, mixed with lumpy material which is evidently not clot, but consists of degenerate cancer cells. Only the smallest arteries and a few of the veins are obstructed.*

Case 9.—F., aet. 37. Cancer of Cervix Uteri, involving parametrium and ovaries. Metastases in peritoneum, inguinal and retroperitoneal glands, and fifth lumbar vertebra. Liver and lungs free from growth. In many of the microscopic arteries of the lungs lies cancerous material sometimes surrounded by thrombotic tissue. Other masses are free in the lumen, and here and there are necrotic in the centre. The arterial wall is never infiltrated.*

Case 10.—F., aet. 47. Carcinoma of Cervix Uteri. A nodule in the omentum. Metastases in the abdominal glands, the bones, and the thoracic duct. No carcinoma visible in the lungs or the pleuræ. Microscopically there are scattered cancerous thrombi in process of organization in the arteries and veins of the lungs. Many veins and a few arteries contain simply cancer cells without any surrounding thrombotic tissue. No growth was seen in the capillaries. No cancer cells were present in the lungs outside the blood vessels.

Case 11.—F., aet. 38. Cancer of the Gall Bladder. Many nodules in the liver. Metastases in the upper lumbar glands, none in the supra-clavicular glands. No naked eye metastases in the lungs, nor other metastases. In every section of the lungs great numbers of the blood vessels, both arteries and veins, are occupied by cancer cells, some of which show mitoses. Some of the cancer cells are surrounded by unaltered red corpuscles, not by a stroma, others by thrombotic material, while yet others are contained in fibrous thrombi. No cancer cells were seen making their way out of the lumen.

Long stretches of the veins are filled with cancer cells, invariably without any stroma formation or thrombus, and without any penetration of the venous wall. Connecting the infected arteries and veins, lines of cancer cells can be seen in the capillaries. No retrogressive metamorphoses of the cancer cells were seen in this case.

Case 12.—F., aet. 67. Carcinoma of the Gall Ducts. Metastases in the liver, abdominal glands, peritoneum. Little pinhead-sized deposits in the lungs.

Microscopically the small pulmonary arteries contain many cancerous thrombi, whose centre is frequently necrotic. Often the vessel wall is being infiltrated. Sections of arteries occur in which the whole lumen is lined with cylindrical epithelium; in others there is fibrous thrombus which encloses cavities lined with regular cylindrical epithelium. Round many of the obstructed arteries the lymphatics contain cancer cells in the form of a flat lining to their interior, in places syncytial in character, replacing the endothelial layer.

Case 13.—F., aet. 29. Carcinoma of Rectum, infiltrating the surrounding organs, and involving the peritoneum. Metastases in the abdominal and left supra-clavicular glands, upon the diaphragm, and at one point of the thoracic duct. None in the lungs, the liver, or other organs. In all sections of the lungs there are many thrombi in the arteries, partly fresh, partly organized and vascular; but in only three arteries are cancerous inclusions found. In the first of these a sickle-shaped lumen remains; the cancerous thrombus, bounded externally by the elastica interna, is separated from the blood stream by a definite layer of endothelium. In the second one the cancer has penetrated to the muscularis. The third is a peri-arterial cancer nodule, of alveolar structure, surrounding the bifurcation of an artery. The artery itself is completely filled by a vascular, non-cancerous connective-tissue thrombus. Schmidt arrived at the conclusion that the original focus was an intra-arterial cancerous embolus, which itself had disappeared, but not before it had penetrated the arterial wall and given rise to the peri-vascular nodule. Partial blocking of the thoracic duct by a cancerous thrombus was found.*

Case 14.—F., aet. 45. Soft Cystic Carcinoma of both Ovaries. Metastases in the peritoneum, and in the pelvic, aortic, portal, posterior mediastinal, and left supra-clavicular lymph glands. Thoracic duct free. Nodules on both surfaces of the diaphragm. Lungs and pleuræ free from growth, right lung almost completely adherent. Death from pulmonary embolism and hæmorrhagic pleurisy.

Microscopically, cancerous foci are widely scattered in the arteries and veins of the lungs. Only those of small calibre ($\frac{1}{4}$ mm. or less) are affected. In the arteries the cancer cells are enclosed in thrombus, and non-cancerous thrombi are also present; but in the veins all the cancer cells are free, and mostly entirely obstruct the vein. Sometimes the peripheral cells form a regular cubical layer lying on the intima, while the central cells are loosely arranged.*

Case 15.—M., aet. 63. Carcinoma of the Prostate. Metastases in the sternum, ribs, and bodies of the first, and seventh to ninth, dorsal vertebræ. A single nodule, 3 to 5 cm. in diameter, was present in the lower lobe of the right lung, and several nodules in the liver. No metastases in the lymph glands nor in the thoracic duct.

Microscopically in the small arteries of the lungs are many occluding fibrous thrombi without definitely cancerous inclusions. Some of the capillaries are obliterated by fibrous tissue. One undoubted group of cancerous cells is present in an arterial thrombus.

In many places the small veins contain groups of coherent cancer cells, lying amid red corpuscles ; in one vein lies a nucleated hyaline thrombus containing cancer cells, in others a clear hyaline substance, made of compressed spherules.

(In cases marked thus * embolic infection of the lungs, and almost certainly therefore of the liver also, had taken place without any development of secondary nodules in these organs, or in the course of the systemic circulation. —W. S. H.)

Schmidt remarks that these 15 cases were not cases of general carcinosis; indeed in most of them the formation of metastases was very limited. The lungs usually appeared to the naked eye quite sound. In five cases not only the lung tissue but the lymph vessels were entirely free from growth.

Syncytia were found in many of the naked cell-emboli, sometimes in contact with the blood, more frequently in the fibrous thrombi. Regressive metamorphoses of the cancer cells could be seen in the recent thrombi. Especially noticeable was the aggregation of small round cells between and in the cancer cells, sometimes lying in a vacuole of their protoplasm. Some of the cancer cells were so completely filled by these round cells that they looked like brood capsules. The nuclei of these round cells, unlike those of the polynuclear leucocytes found in small numbers in the surrounding fibrous thrombus, consisted of isolated balls of chromatin. In a large cancerous focus the entire centre may be destroyed and occupied by a mass of such round cells. The present writer has often noticed this leucocytic invasion of the central degenerate portion of a mass of cancer cells.

Schmidt's general conclusions had better be given in a translation of his own words. It will be seen that he remains an advocate of the embolic theory :—

> "In carcinoma of abdominal organs cancerous embolism of the small arteries of the lungs occurs with unlooked-for frequency and often repeatedly. Only a small proportion of these emboli give rise to metastatic tumours, or break through the arterial wall into the perivascular lymphatics. Most of them are either destroyed by organization of their ensheathing thrombus, or while retaining the power of growth are encapsuled and rendered harmless. They may, however, push forward through the organizing thrombus which surrounds them into the capillaries and small pulmonary veins, and may so give rise to growths in the course of the systemic circulation. All this may happen while to the naked eye the lung remains unaltered."

It must be pointed out that Schmidt's work, careful though it is, embodies a source of fallacy which he has not recognized. As I shall show, a cancerous lymphatic, as the result of perilymphatic fibrosis (see p. 85), very frequently undergoes destruction and is replaced by a fibrous cord, not recognizable as a lymphatic. It is possible that in some of Schmidt's cases the lungs were primarily invaded by way of the lymphatics, and that the cancerous lymphatics, after locally infiltrating the wall and invading the lumen of the neighbouring veins and arteries, subsequently disappeared. This criticism could be effectively met by artificial lymphatic injections demonstrating normal lymphatics near the cancerous emboli within the blood-vessels.

Subject to this criticism it may be admitted that Schmidt's striking work has demonstrated the frequency of embolic blood-invasion. Dr. Bashford* has also drawn attention to cancerous embolism of the pulmonary arteries in the form of carcinoma which occurs in mice.

Cancerous embolism of the lungs has not been demonstrated in breast-cancer, though probably it sometimes occurs. It is worth noting that Schmidt's 43 cases included two of

* Scientific Reports of the Investigations of the Imperial Cancer Research Fund, No. 2, Part ii., p. 38.

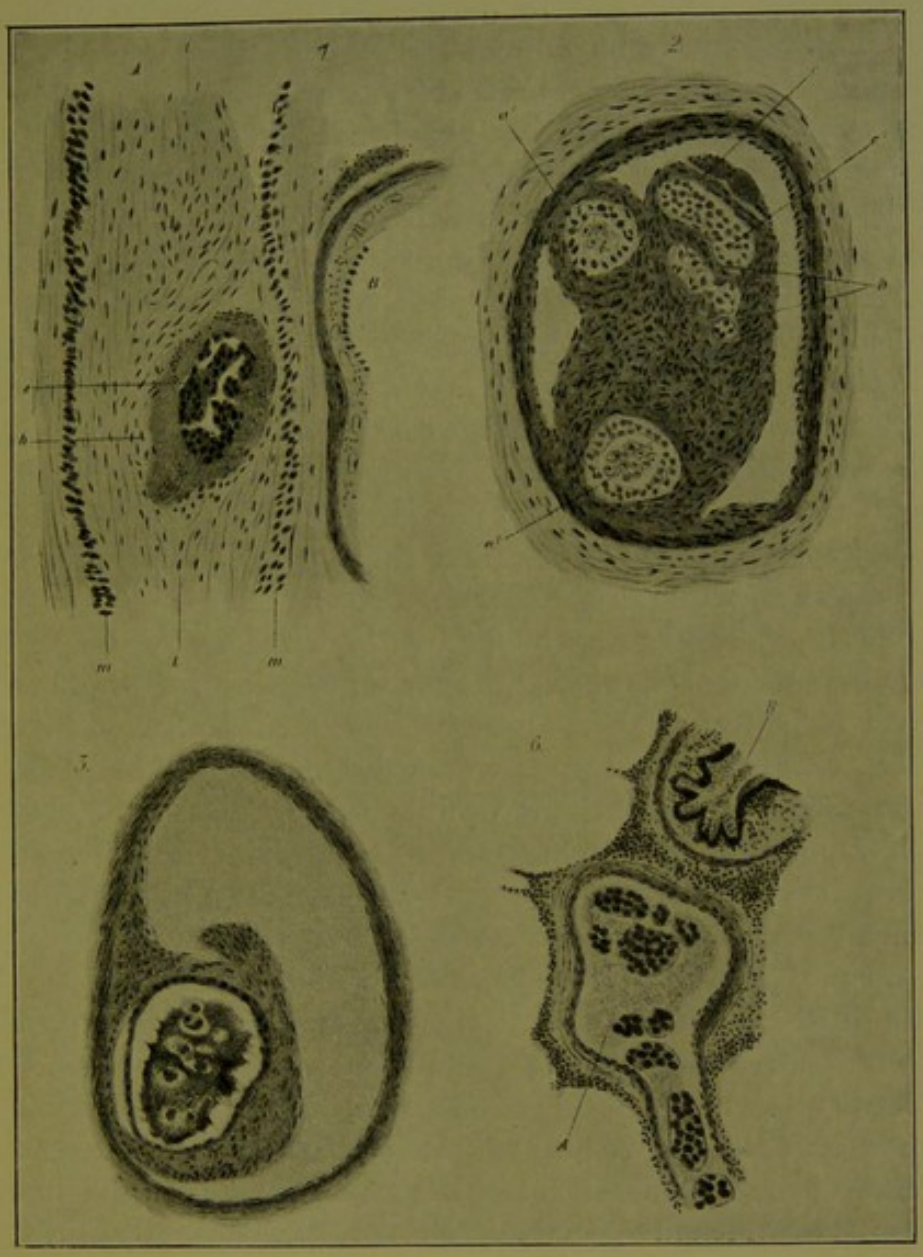


FIG. 1.—(M. B. SCHMIDT). THE DESTRUCTION OF CANCEROUS EMBOLI LODGED IN THE SMALLER PULMONARY ARTERIES.

1.—An artery, A, partially blocked by an old organized thrombus, *t*. The remaining part of the lumen is blocked by a recent fibrinous thrombus, *h*, containing a group of cancer cells, *e*. B is an adjoining bronchus.

2.—An artery containing a connective-tissue thrombus in which are small groups of degenerate cancer cells in process of destruction.

3.—An artery partially blocked by organized thrombus, containing a mass of degenerate cancer cells, only the peripheral layer of which is well preserved.

6.—Recently lodged cancerous emboli lying free in the blood in a small artery, A, above which is seen a bronchus, B. No thrombosis has yet taken place around the cancerous emboli.

breast cancer, and that in neither of these was he able to demonstrate cancerous pulmonary embolism.

In order, however, to establish the embolic theory it is necessary to show that this blood-invasion is *effective*. So far from this being the case, Schmidt's work shows that, as a rule, cancerous epithelium which reaches the blood stream is either destroyed or rendered incapable of growth. If the tissues were arranged in order of specific resistance to cancer, it seems probable that, next perhaps to cartilage, blood would take the highest place.

In twelve of Schmidt's fifteen cases of cancerous pulmonary embolism the lungs remained free from macroscopic nodules. Only three showed secondary deposits in the lungs visible to the naked eye. In two of these three cases miliary nodules were present, while in the third a solitary nodule was present in one lung. Even in the lungs, then, the chances against the *success* of a cancerous invasion by way of the blood appear to be five to one. It may indeed be said that in the twelve cases where naked eye metastases failed to develop the invasion was recent, and would have ultimately succeeded. Such an argument defeats itself, for if blood-invasion only occurs at the doors of the post-mortem room, it evidently cannot be an important factor in dissemination.

We may now study the question what metastases actually arose in Schmidt's fifteen cases along the course of the systemic circulation from the potential cancerous emboli present in the lungs. If we take away deposits in the lymph glands, metastases within the abdominal cavity, where the primary growth was situated, and metastases in the lungs themselves, only five cases show metastases still requiring explanation :—

Case III.—A nodule near the thoracic duct, opposite the fourth dorsal vertebra (probably a lymphatic gland).

Case VI.—Nodules on the pleura (associated with nodules on the under-surface of the diaphragm).

Case X.—Multiple nodules in skeleton. Thoracic duct invaded.

Case XIII.—Nodules on the upper surface of the diaphragm ; the peritoneum showed deposits.

Case XV.—Multiple nodules in the skeleton.

A careful study of these cases will show that, two cases excepted, all the metastases present can be easily and naturally accounted for by lymphatic dissemination. As regards Cases X. and XV., in which bone metastases were present, I shall be able to show that in all probability even distant metastases in bone are frequently the result of lymphatic, not of blood, dissemination.

Schmidt's work shows why cancerous epithelium as a rule fails to colonise the blood stream. The cancer cells excite thrombosis, and the thrombus as it organises and contracts destroys them. Goldmann found that thrombosis might even precede the actual cancerous invasion of a vein. He also showed that invasion of the veins near the primary growth might occur in cases which were found post mortem to be entirely free from metastases. Schmidt found thrombotic material round some or all of the cancerous emboli in the lungs in fourteen out of fifteen cases, and round all of them in seven cases. He was able to trace all the stages in the destruction of cancerous emboli of the lungs. In one case particularly there were numerous arterial thrombi apparently the result of cancerous embolism, though at only one point were recognisable cancer cells still present within a thrombus. In the remaining case of the fifteen all the cancerous emboli were devoid of thrombotic covering, yet even in this case the only other visceral metastases occurred in the liver, and were therefore the cause and not the consequence of the cancerous invasion of the lungs. It is somewhat surprising, in view of the evidence he has himself collected, that Schmidt remains a supporter of the embolic theory. I cannot help thinking that the authors who have investigated the embolic theory only adhered to it because in spite of its difficulties no alternative theory presented itself.

In showing that cancer cells in blood excite thrombosis, and that the thrombus as it organises usually destroys or renders them harmless, Goldmann and Schmidt seem to have established a fact of primary importance, and one which is strongly opposed to the embolic theory as applied to carcinoma. Cancer in lymphatic vessels, as far as I have seen, excites no such thrombosis, a fact to which Schmidt himself

draws attention. Hence it is no doubt that although carcinoma often obtains access to the blood almost as early as to the lymph, its dissemination takes place almost entirely by the lymphatics and not by the blood vessels.

It is a significant fact that chorion-epithelioma, the only carcinoma certainly known to spread habitually by the blood, ends oftener in spontaneous cure than does any other form of carcinoma. In a series of 188 cases of chorion-epithelioma Teacher* records four instances of apparently complete recovery following an incomplete operation, and eight other cases in which, though haemoptysis indicated lung metastases, removal of the uterus was successful in restoring the patient to health. It would be easy to adduce other arguments against the embolic theory. Frequently the thorax is found full of secondary growths while the abdomen is entirely free from them. Just as frequently the converse is the case. Now, as Mr. Stephen Paget has insisted, blood embolism must by its very nature be an indiscriminate process; the cancerous emboli must be distributed impartially to all the organs. Why then in certain cases do the cancerous emboli gain a footing only in the abdominal organs, and in other cases only in the thoracic organs? The hypothesis of tissue-predisposition does not meet the difficulty, unless the assumption be made that in some cases the abdominal organs are predisposed to cancer and the thoracic ones resistant, while in other cases the exact reverse obtains. Such a supposition must I think be regarded as the "last ditch" of those who defend the embolic theory.

What conclusions then do we reach as to the truth or falsity of the embolic theory? Quite clearly it is not, standing alone, an adequate and complete explanation of all the remote metastases in cancer. As will appear later, my own work has demonstrated that the subcutaneous nodules so frequently seen in breast-cancer are due, not to blood embolism, but to the growth of cancer along lymphatic vessels (permeation). I have also shown that the peritoneal and pleural cavities are invaded, frequently at any rate, if not invariably, by lymphatic permeation, and that the dispersion of cancerous particles through the serous cavities is

* Teacher, *Journal of Obstetrics and Gynæcology*, July and August, 1903.

a very important factor in dissemination (Chapter V). Furthermore there is strong *primâ facie* evidence from the distribution of bone metastases that these also are not the result of embolism by way of the blood stream.

Blood-embolism, far from being a dominant and universal factor in the dissemination of breast-cancer, appears to be an event of exceptional occurrence, and one which, even when it occurs, is usually rendered ineffective by the destruction of those cancer cells which gain access to the blood stream. In rare cases it doubtless leads to the formation of secondary nodules. But the peculiarities of metastastic distribution, which will later be further referred to, indicate that it is quite subordinate in importance to the process of lymphatic permeation.

CHAPTER II.

A CLINICAL AND MACROSCOPIC STUDY OF PARIETAL DISSEMINATION.

External (Parietal) and Internal (Visceral) Dissemination.

THE secondary deposits which occur in breast-cancer may be considered under two headings; first, those which occur in the parietes and in the limbs, that is to say in the skin, subcutaneous tissue, deep fascia, muscles, and bones; secondly, those which occur within the thoracic or abdominal cavities, or in the central nervous system.

This anatomical division of the metastases corresponds to the two forms of dissemination, parietal and visceral, which occur in breast-cancer. They usually occur in combination, but that the distinction is a natural and not an artificial one is clearly proved by such cases as those of Arnott,* and of Walther,† and by a case of which a model exists in the museum of St. Thomas's Hospital (see Fig. 8). In these instances there were multiple and widespread metastases in the bones or in the bones and subcutaneous tissues, while the internal organs were free from cancer.

Out of 470 autopsies on breast-cancer at the Middlesex Hospital, Campiche and Lazarus-Barlow‡ found no fewer than eleven cases in which secondary deposits occurred only in the skeleton. The occurrence of such cases is extremely difficult to explain on the embolic theory, and suggests that visceral dissemination is a secondary and not invariable consequence of parietal dissemination, and that the latter should be the primary object of study. This chapter will therefore be devoted to a clinical and statistical study of parietal dissemination.

* Arnott, Trans. Path. Soc., Vol. xix., p. 356.

† Walther, Bull. de la Soc. Anat., 1890, p. 423.

‡ Archives of the Middlesex Hospital, Vol. v., 1905, p. 97.

Parietal Dissemination a Centrifugal Process.

When a few scattered nodules of cancer are found in the skin near the breast-cancer, or when the adjacent ribs or sternum show cancerous nodules, no difficulty is felt in attributing these to local lymphatic spread. But when subcutaneous nodules are present over the greater part of the surface of the body, or when distant bones such as the femora or the cranium are attacked, the hypothesis of centrifugal lymphatic spread is abandoned for that of embolic blood invasion. There is in my opinion no sufficient reason for this change of attitude.

That centrifugal spread may annex by continuity a very large area round a carcinoma is convincingly shown by cases of cancer *en cuirasse* such as that recorded by Velpeau in the following graphic description :—

> Among the unhappy women I have seen in this state, I may single out an English lady, whose integuments from the flanks to the neck, from the umbilicus to the larynx, from the loins to the occiput, had undergone this brawny (ligneuse) change. Her skin, moreover, as far as the axilla and the shoulders, was sown with scirrhous ulcers and closely set cancerous bosses. The breathing of this poor woman, whose two arms were tripled in bulk and as hard as marble, was so shallow that it resembled that of a strangled person, or of one whose chest is gripped in a vice ; she could move neither her arms nor her head, her pain was constant and frightful. When I saw her with Dr. Skiers. her medical attendant, she indeed presented a pitiable sight, uttering piercing cries, calling for death but powerless to compass it, and praying for a dose of opium to end her sufferings.

In a recent paper*, which is here reproduced and supplemented, I brought forward *primâ facie* evidence that cancer of the breast slowly spreads centrifugally and by continuity from its seat of origin in a way that recalls the mode of spread of erysipelas, though not in the same plane. The area of extension in both instances is rather bounded by two dimensions than by three, and tends to assume a circular form, with the primary focus as centre. Thus, erysipelas spreads essentially in the plane of the skin, and carcinoma

* "The Centrifugal Spread of Mammary Carcinoma in the Parietes, and its Bearings on Operative Treatment," Archives of the Middlesex Hospital, Vol. iii., 1904, p. 27.

often shows a tendency to spread widely in the plane of the parietes, before involving the internal viscera.

Leaving aside the embolic infection of the axillary glands, the infected area of the parietes as the growth advances might be represented roughly by circles of ever increasing radius centred on the primary growth. In some cases centrifugal extension may ultimately involve the greater part of the surface of the body. It appears to take place quite independently of any transport of cancer particles by the blood or lymph streams, and rather proceeds by direct growth along the finer lymph vessels (permeation).

Centrifugal Extension in the Parietes.

There are five layers in which evidence of the centrifugal extension of mammary cancer may be sought. These are—

(i) The skin.
(ii) The subcutaneous fat.
(iii) The deep fascia.
(iv) The muscles.
(v) The bones.

Since, however, subcutaneous nodules affect both the skin and the subcutaneous fat at the same time, and since little is known of cancer in muscle, the layers to be considered are practically reduced to three—

(i) The skin and subcutaneous fat.
(ii) The deep fascia.
(iii) The bones.

The secondary deposits in each of these layers must now be considered separately with regard to the question of centrifugal spread.

(i) *The Skin and Subcutaneous Fat.*

It is almost an axiom in the present day pathology of breast-cancer that the skin is early infected, and that cancer extends along it in all directions from the primary growth. The subcutaneous nodules which so frequently appear in the neighbourhood, and may later involve a very wide area round it, are often regarded as conclusive evidence on this point. Discussion of this view may for the present be deferred.

Careful observations on the appearance and spread of skin nodules are hard to find. It seems, however, quite certain that, as Velpeau first stated, these nodules always make their earliest appearance in the immediate neighbourhood of the primary growth. They are very rarely, if ever, found on the scalp, the upper arm, or the abdomen until some time after they have made their appearance on the front of the chest.

Mr. Stanley Boyd,† in a paper on Oöphorectomy for Breast Cancer, gives three very careful sketches of the same case at different periods. The centrifugal extension of the area in which skin-nodules occur is clearly manifested. The growth was in the right breast. At first about five subcutaneous nodules were seen on the affected side of the front of the chest, near the operation scar. Next a nodule appeared at the anterior edge of the right latissimus dorsi. Later, nodules appeared in the right upper arm, at the right scapular angle, over the left side of the front of the chest, and in the skin of the abdomen over the epigastric angle. In a late stage the nodules became so numerous over the front of the abdomen nearly down to the pubes that it was impossible to chart them. A case recorded by Dr. Byrom Bramwell‡ illustrates very well how, as the case progresses, subcutaneous nodules appear at points successively more and more remote from the primary growth.

The following two cases from the records of the Middlesex Hospital also illustrate the spread of subcutaneous nodules in the region surrounding the primary growth :—

In the first case the left breast presented a surface which was raised and ulcerated in part, and the skin around was nodular from the existence of numerous subcutaneous deposits of new growth, which extended over the front of the left half of the chest in its upper part, and also over and above the right clavicle. In a backward direction these deposits could be detected nearly to the posterior axillary fold. The left shoulder was covered by this subcutaneous nodulated growth, and was almost fixed. (P.M. Register, 1901, No. 59.)

†"On Oöphorectomy in the Treatment of Cancer of the Breast," Boyd. (*British Medical Journal*, February 4th, 1899, p. 257.)

‡Byrom Bramwell, *Edinburgh Medical Journal*, July and August, 1894. A summary of this case will be found on p. 143.

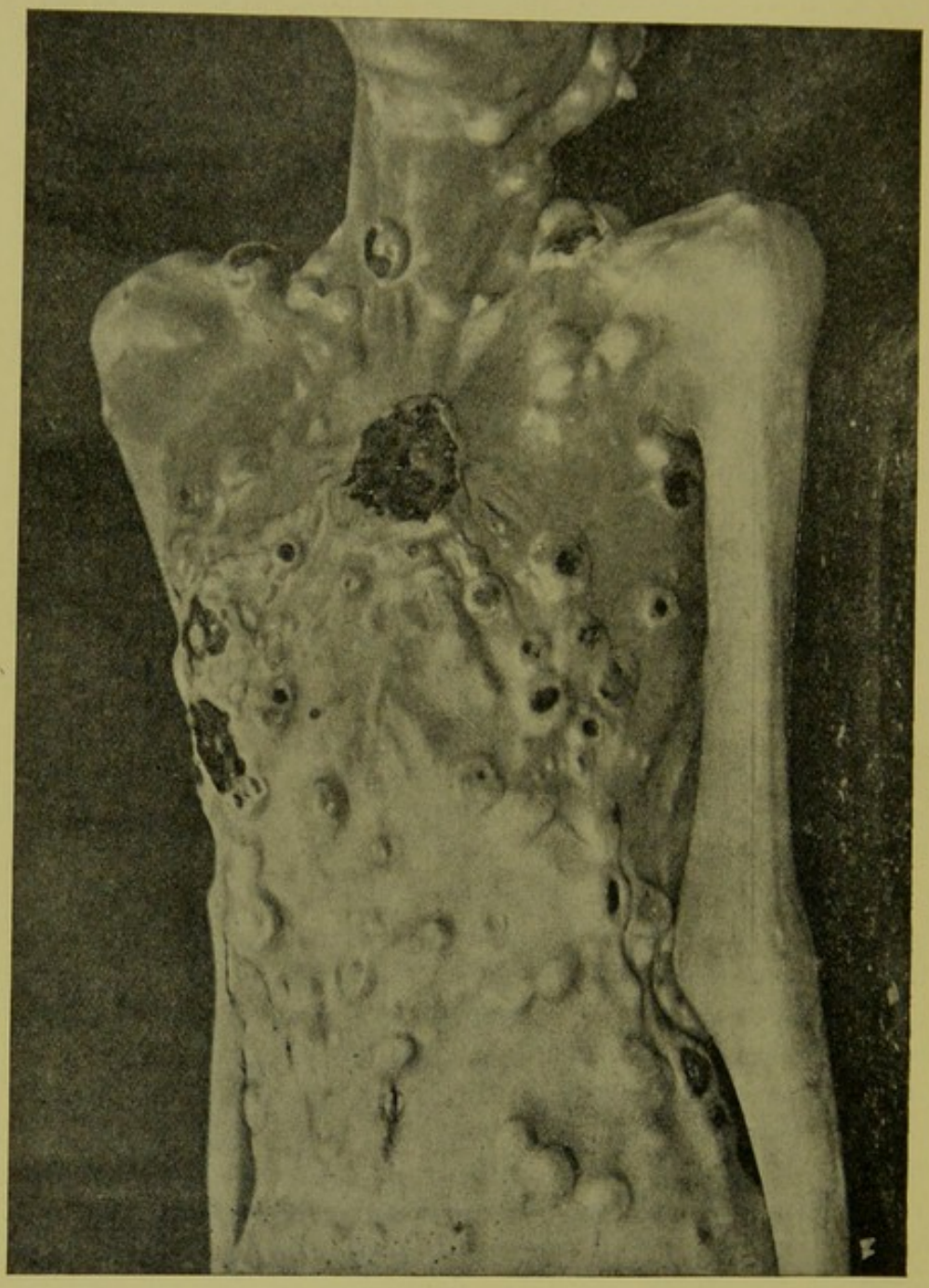


FIG. 2.—A CASE SHOWING VERY EXTENSIVE CENTRIFUGAL SPREAD OF SUBCUTANEOUS NODULES. (THE MIDDLESEX HOSPITAL.)

Note the comparative immunity of the limbs, and the ulceration of the larger nodules. A mass of confluent ulcerated nodules is seen on the front of the chest.

The other case showed a wider distribution of skin nodules, but nevertheless the distal portions of the limbs were free. There was great wasting, and the body presented a remarkable appearance owing to numerous large (1–2 inches diameter) secondary growths in the skin. These growths occurred principally on the front of the chest and abdomen, but were also present on the back, the face, behind the jaw, the eyelids, and the limbs. In the latter situation it is especially noted that the chief distribution was on the parts near the trunk.

Many of the nodules on the chest were ulcerated; others were rounded and projected for nearly an inch. A large growth was situated over the sternum, and thence indefinite lines of nodules seemed to radiate in all directions. About an inch to the right side of the linea alba, and parallel to it, was a conspicuous line of nodules. In most instances the nodules were subcutaneous, and did not extend to the deeper layers of the parietes. No deposits were found in the lungs. (P.M. Register, 1902, No. 52.) Fig. 2 represents this case.

Mr. (now Sir Frederick) Treves in the *Lancet* for Sept. 10, 1887, recorded a case of scirrhus of the breast with numerous nodules beneath, but not adherent to, the skin.

Ten months before the patient's admission under his care, when two months pregnant, she noticed a small round nodule in the right breast. Two months later a similar nodule appeared in the left breast. On admission, the centre of the right breast was occupied by a hard mass consisting of loosely-connected marble-like nodules, adherent to the skin. The tumour was fixed to the underlying pectoral muscle. For a considerable distance round the mamma, the subcutaneous tissue was occupied by widely disseminated nodules. The majority of these lay between the breast and the axilla; some extended as high as the clavicle, others reached the middle line, while some were found scattered over the upper part of the abdomen. The skin over these nodules was normal and non-adherent. Their size varied from a small shot to a bean. The largest were near the heart, and the further the distance from the nipple, the smaller the nodules became. Over a hundred of them were present. A peculiar nodular cord ran from the mamma to the axilla, where it was lost. The nodules were roughly grouped along lines that radiated from the nipple. The axillary and supra-clavicular glands were enlarged on the right side only. The left breast was occupied by a growth like that in the right, but not adherent either to skin or muscle. Around it were some sixty nodules like those already described, but not extending so far from the breast. None of

them had reached either the clavicle, the axilla, the middle line, or the skin of the abdomen. The patient had never suffered pain. The nodules had appeared in crops, extending from the nipple area.

Sir F. Treves remarks that the case appears to show in an exaggerated way the mode in which a scirrhus extends. He compares the mode of extension to the lymphatic spread of pulmonary tubercle, and of lymphadenoma. The case evidently strengthens the view that skin nodules are the result of centrifugal spread. It appears to be a true instance of primary carcinoma of both breasts.

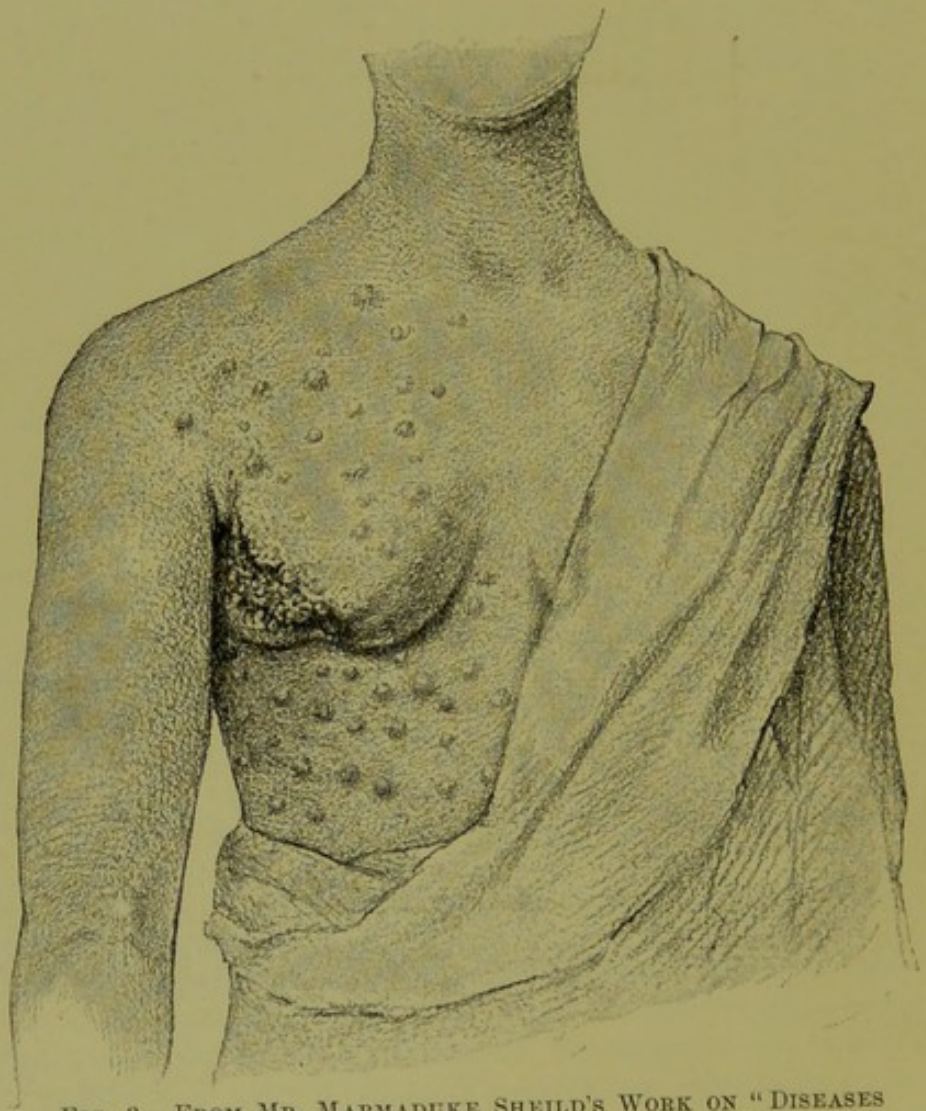


FIG. 3.—FROM MR. MARMADUKE SHEILD'S WORK ON "DISEASES OF THE BREAST."

The drawing is reproduced here to show how skin nodules have spread from the primary growth in all directions, involving an area around it which is roughly circular.

The annexed drawing of a case of Mr. Marmaduke Sheild's (Fig. 3), which he has kindly allowed me to use, is Fig. 55 in his well-known work on "Diseases of the Breast." I am greatly indebted to him for permission to reproduce it here. It depicts a middle stage, or a moderate degree, of the process of nodule formation. The nodules have spread centrifugally so as to involve a considerable circular area round the growth. They have extended rather more widely in a vertical than in a horizontal direction, and this appears to be a general rule.

In the following case the nodules extended over a wider area, but the centrifugal process of spread as it receded from the primary focus seems to have lost some of its virulence, so that the peripheral nodules were few in number and sparsely scattered.

Necropsy No. 176, Middlesex Hospital, 1905. The examination was made by Mr. Cecil Rowntree, to whom I am indebted for the careful measurements and diagrams:—

The patient was an emaciated woman, aged 80. In the situation of the right mamma was a deep ulcer 2½ inches in diameter, and nearly circular in outline. Extending in all directions around the ulcer were small discrete patches of new growth in the skin. Scattered more sparsely over the body were other nodules in the subcutaneous tissue freely movable under the skin. All the nodules present are figured in the diagram, which also gives the distance of the nodules in inches from the edges of the ulcer. The left breast was normal; the nodule represented in the diagram was in the subcutaneous tissue superficial to the breast. (See Fig. 4.)

Very numerous nodules the size of peas were scattered throughout both lungs. There was one small deposit on the right pleura in its upper part; no fluid in the pleural cavities.

In the peritoneum over the bladder, almost in the middle line, was a small nodule, apparently of secondary carcinomatous nature. In the neighbourhood of the right crural ring was another peritoneal nodule, which apparently had become attached to the lymph-gland in the crural canal.

Moderate violence did not produce any fractures of bones. The clavicles, ribs, and bodies of the vertebræ were demonstrated to be free from growth. There was slight lateral curvature with the concavity to the right. The vault of the skull was infiltrated with new growth, which, however, was chiefly confined to the diploë, only two small areas being raised above the general surface externally, and none internally.

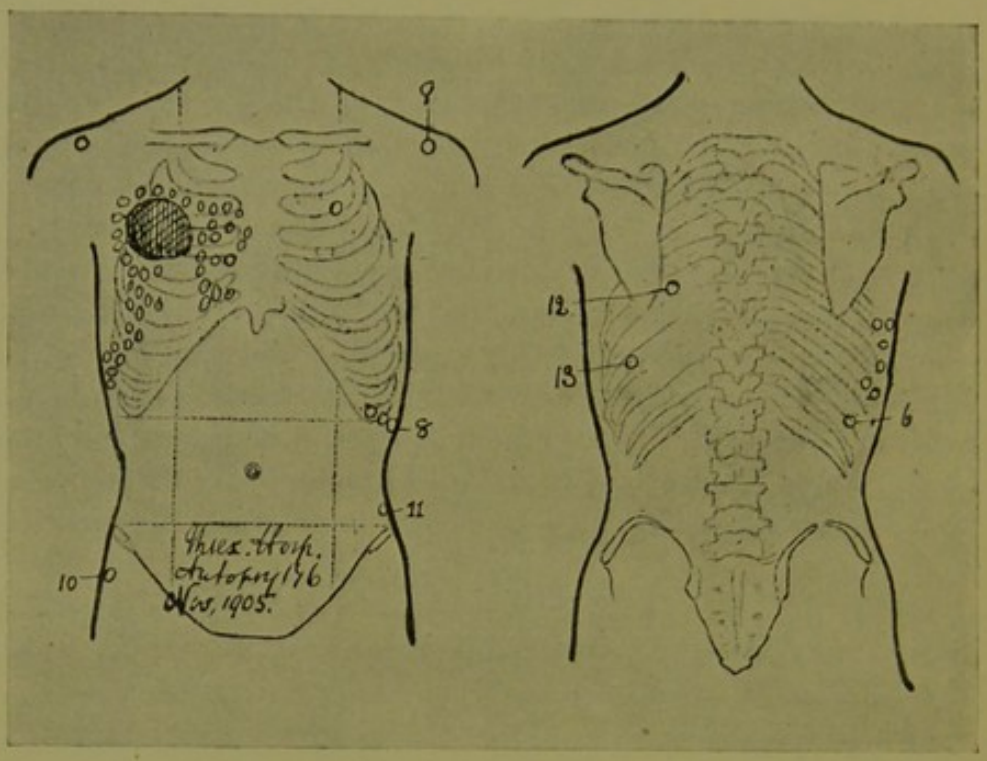


FIG. 4.—FROM A RECENT AUTOPSY ON BREAST CANCER AT THE MIDDLESEX HOSPITAL

showing all the subcutaneous nodules which were present. The limbs were entirely free from nodules. The figures indicate the distance of some of the nodules in inches from the edge of the primary growth.

REMARKS.—Mr. Rowntree has in several cases of breast-cancer observed lateral curvature without rotation. In all cases the concavity of the dorsal curvature has been towards the side of the primary growth. He believes the curvature to result from the contraction of the primary growth. The observation is an interesting, and I believe a novel one.

The case illustrates very well the centrifugal spread of permeation, for all the nodules lay within a circle of approximately ten to twelve inches in diameter. Moreover, all the remoter nodules were free from adhesion to the overlying skin. This is frequently the case: a strong argument in favour of the fascial rather than the cutaneous spread of breast-cancer.

The nodular metastases in the lungs, if one may judge by their uniform distribution, and by the freedom of the pleural cavity, arose from blood embolism.

The pelvic nodules of secondary growth were probably the earliest indication of epigastric invasion (see p. 130). Gravity evidently had much to do with their position.

The most extreme instance of widely disseminated skin-nodules I have found is one recorded by Dr. Rolleston.* The primary growth was a small one in the lower and outer part of the left breast, and the breast was removed, along with two glands in the left axilla, which were found to be carcinomatous. Twenty-one months after the operation a small nodule was noticed under the skin over the right clavicle. Subsequently very numerous nodules developed. A year after the first recurrence there were 105 of these, together with a mass in the right mamma. Four months later, following the administration of arsenic and thyroid extract, the number of nodules had diminished to 78. The glands in the axillae and groins were enlarged.

The distribution of the nodules is illustrated in two figures, one showing the front, the other the back of the body. The figures afford very strong evidence for centrifugal spread, in that *the arms below the middle of the humerus, and the lower limbs below the upper third of the femur, are entirely free from nodules.* In Dr. Rolleston's opinion the nodules had become disseminated by the blood stream, but such a hypothesis seems quite inconsistent with the entire escape of the distal extremities of the body, the regions where the circulation is terminal, and where non-cancerous embolism at all events produces its most characteristic effects.

It is true that there are numerous nodules in the scalp which could be explained by embolism, but the hypothesis is unnecessary. By marking the position of the most remote nodules in Dr. Rolleston's diagrams on the skin of a living subject, and taking actual measurements by the shortest route along the skin surface, it was found that the uppermost nodule, i.e. one on the scalp in front, was about 21 inches distant from the situation of the left nipple. The most remote nodule downwards, that in the right groin, was 22 inches from the same point. The nodule furthest to the right, when the right arm was raised, was 18 inches from the left nipple; that furthest to the left, on the left arm, was 14 inches from the left nipple. Many of the nodules on the

* "A Case of Multiple Cutaneous Carcinomatosis after Carcinoma Mammæ," by H. D. Rolleston, M.D. (Clinical Society's Transactions, Vol. xxxiv., 1901, p. 206.)

back, measuring around the thorax either to right or left, were between 15 and 17 inches distant from the left nipple. Indeed, on the posterior aspect of the trunk the edges of the infection circle, serpiginous by reason of the irregularities of the surface, seem clearly traceable as its opposite convexities wrap round the body and tend to meet towards the right side of the back. The parts of the back most

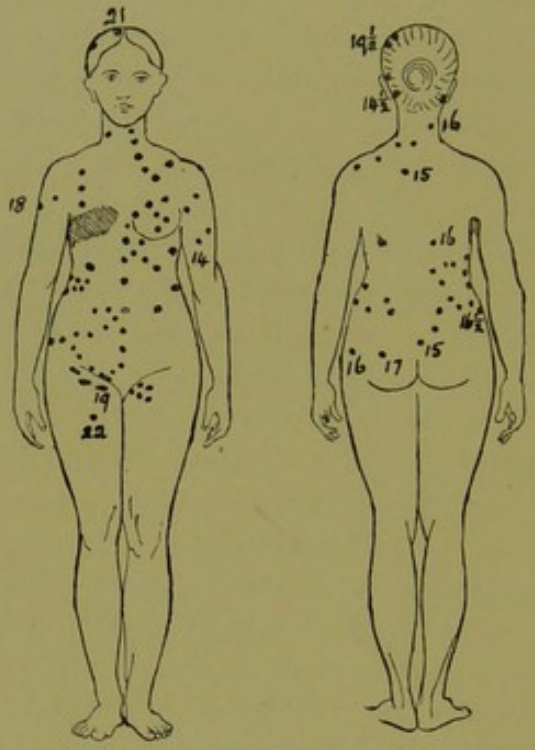


FIG. 5.—DIAGRAM SHOWING THE DISTRIBUTION OF THE SUBCUTANEOUS NODULES IN DR. ROLLESTON'S CASE.

The *left* breast was previously removed for carcinoma. The shaded area over the right mammary region represents a number of closely packed secondary growths. The figures attached to certain of the nodules represent their distance in inches from the left nipple, measured by the shortest route along the skin surface.

The writer is indebted to Dr. Rolleston for permission to use this diagram.

remote from the left nipple are free from nodules. These parts are, of course, the right scapular and the right gluteal regions.

If we assume that a small part of the primary growth was left behind about two inches internal to the left nipple, and just below it, all the nodules fall just within an oval area of 21½ by 16 inches, having this point as centre, and with its long axis vertical. They have spread just as much upwards

as downwards, and just as much to the right as to the left. It must, however, be admitted that within the nodule area their distribution is somewhat irregular, as is evidenced by the escape of the face and much of the left side of the abdomen. The point, therefore, upon which chief stress must be laid as an indication of centrifugal spread is the absolute immunity of the parts of the body beyond the area indicated, i.e. the distal portion of the limbs.

The distribution of skin nodules over an approximately circular area of very variable size, with the primary growth at its centre, is evidently not accidental but characteristic, and the area involved in the most extreme recorded cases is only an extension of the circle of invasion so clearly shown in Mr. Sheild's case. The limbs escape, no doubt, simply because the patient dies before the slow centrifugal spread of the growth has time to extend to them.

It will be found that, as a general rule, the nodules near the primary growth are the largest, and those further away are smaller in size, and less closely adherent to the skin. In some rare cases, as in one recently at the Middlesex Hospital, skin nodules may ulcerate (see Fig. 2). It is noticeable that the ulceration is most marked in the immediate neighbourhood of the primary growth. These facts all support the centrifugal hypothesis, since they show that the oldest nodules lie near the centre of the invaded area of skin, the most recent ones near its periphery.

Of course it is not for a moment suggested that the very extensive parietal dissemination which these cases show is anything but a late and rare event, or the operative treatment of breast-cancer would indeed be a hopeless task. They are inserted here to show that even when parietal dissemination is seen in its last stage, and in its greatest extent, all the parietal metastases occur within a ring-shaped area whose centre is the primary growth. The inference is that in the average case of breast-cancer, in the early operable stage before any subcutaneous nodules have appeared, there is microscopic cancerous invasion of a similar, but of course much smaller annular area of the parietes around the growth. As will later appear, direct microscopic examination confirms this conclusion.

Cases of extensive subcutaneous nodular deposits, when not ascribed to embolic dissemination, *via* the blood stream, have usually been explained upon the assumption that the carcinoma extends in the "deep cutaneous plexus" of lymphatics at the junction of the corium and the subcutaneous tissue. But no satisfactory proof of this supposition, nor even of the existence of the "deep cutaneous plexus," has yet been brought forward (see p. 47).

The irregular distribution of subcutaneous nodules within a regular area seems rather to indicate that they are accidental efflorescences of growth which is really extending in a deeper plane. It may be that they are simply the index of continuous spread of growth in the deep fascia.

In this connection it is worthy of note that, though Stiles was able to demonstrate cancerous lymphatics in the connective-tissue septa which unite subcutaneous nodules to the deep fascia, he has brought forward no microscopic evidence of any continuity of infection *along the skin* between neighbouring nodules.

The fallacy of arguing that because subcutaneous nodules spread centrifugally from the growth, therefore the growth necessarily spreads along the skin, may be illustrated by the annexed diagram.

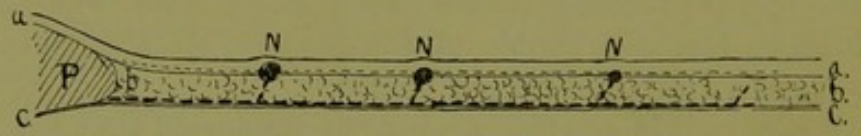


FIG. 6.—TO SHOW THAT SUBCUTANEOUS NODULES DO NOT NECESSARILY ARISE FROM THE EXTENSION OF GROWTH ALONG THE SKIN.

The diagram represents a section of the parietes at right angles to the surface in the region of the primary growth P : a a skin, b b subcutaneous fat, c c deep fascia. The subcutaneous nodules N N N may arise (1) from spread of growth in the skin in the direction of the lightly-dotted line, a view generally held ; *or* (2) from spread of growth in the deep fascia, along the heavy interrupted line, with occasional offshoots to the skin, giving rise to subcutaneous nodules. Though this is not the accepted view, it is the correct one in the writer's opinion. Cf. Fig. 47, p. 208.

While it is quite possible that the growth spreads along the skin in the direction of the light dotted line, subcutaneous nodules may equally well be explained by extension of the growth in the deep fascia, along the heavy dotted line, with lateral extensions here and there towards the skin.

The question along which of the planes of the parietes breast cancer *primarily* spreads must be deferred until infection of the deep fascia, and of the bones, have been considered.

(ii) *The Deep Fascia.*

It is not the object of the present chapter to consider the microscopical evidence for the spread of cancer along the fascial lymphatic plexus. It can, however, be traced to some extent macroscopically by the following method, which has the advantage of rendering visible the coarser ramifications of the growth in the parietes in pieces of some thickness, while the microscope shows only one plane. This method is the result of numerous experiments which I have made. It has been recently modified and improved (see Appendix, p. 206).

1. The tissue to be examined is fixed for a few days in a five per cent. solution of commercial formalin.
2. A thin slice, vertical to the surface, is cut from it, a step much facilitated by freezing the tissues. The slice should not exceed 3–4 mm. in thickness, but may be of any length. Along one edge will be seen the skin, below this the subcutaneous fat, and the subjacent deep fascia and muscle.
3. This slice of tissue is stained for a week in a fluid consisting of nine parts of Müller's fluid to one part of formalin (Orth's fluid). The fluid requires changing several times. If a granular deposit forms on the surface of the slice of tissue, it should be washed in running water.
4. The specimen is washed in water and transferred to absolute alcohol through methylated spirit.
5. When dehydrated, it is transferred to xylol, or to cedar-wood oil, and permanently preserved in the medium.

There is unfortunately no specific stain for carcinomatous epithelium ; and in the main this method simply differentiates protoplasm from its connective-tissue products. But in some situations, and especially in the parietal tissues, no

more is required. The specimen obtained by this method should be examined by strong transmitted light. The protoplasmic tissues are stained in various shades of reddish-brown, while the fat, which is rendered translucent, remains practically unstained. Cancer in the deep fascia or in muscle stains a reddish-brown, while normal muscle stains a darker brown. The method is not very advantageous for tracing cancer in the skin which itself is somewhat stained.

Not only are cancer nodules in the fat, fascia, or muscle, rendered plainly visible, but the larger cancerous lymphatics are seen as ramifying dark lines. (See Frontispiece and Fig. 7.) In my hands this method has given better results

FIG. 7.—Photograph × 3, with key-diagram attached, shows a late stage of cancerous invasion of the deep fascia round a carcinoma of the breast. It represents a horizontal slice of tissue ½ inch thick taken from the upper part of the abdominal wall. The specimen is viewed by transmitted light. The skin at this level was free from obvious growth, though subcutaneous nodules were present higher up. Above is seen the subcutaneous fat, separated from the rectus muscle by A A, the anterior layer of the rectus sheath. The dark masses marked B are cancer nodules which originated from growth lying within the vessels of the fascial lymphatic plexus. Here and there they are sending prolongations towards the skin.

The specimen was stained and rendered translucent by the method described in this Paper. For the photograph I am indebted to Mr. A. Smith of the Samaritan Hospital.

than the nitric acid method of Stiles. By means of it the extension of cancer along the deep fascia can be demonstrated in those cases where macroscopic fascial nodules are formed.

(iii) *The Bones.*

During the thirty years 1872–1901 there have been at the Middlesex Hospital 329 autopsies on cases of mammary carcinoma. Excluding cases where the only bones to which cancer had extended were the sternum or the ribs, there were 37 cases in which the bones were the seat of secondary deposits, or of spontaneous fracture. Including cases where the primary growth had invaded the sternum or the ribs, this total is raised to 73 cases.

The statistics derived from these cases do not afford very reliable information as to the frequency with which different bones are affected by secondary growths.

Speaking generally, post-mortem statistics only afford trustworthy evidence of the frequency of metastases in those bones which are liable to spontaneous fracture. A complete examination of the skeleton is made very rarely indeed, and as a rule the pathologist's attention is not directed to more than the vertebral column unless fractures of the long bones are present.

The flat bones may be extensively cancerous without breaking, and the escape of the scapula and the pelvic bones from cancerous deposit is almost certainly apparent only. The flat bones of the skull, which usually come under notice during the examination of the brain, are not infrequently found to be the seat of secondary growths, and it would therefore be unsafe to argue that the scapula and the os innominatum are not similarly liable to metastases.

The case of the long bones is different. Whenever a long bone is extensively cancerous, fracture of it is almost certain to occur sooner or later. Not infrequently, indeed, fractures occur when the body is being actually moved on the post-mortem table. If, therefore, no mention of certain long bones as being either the seat of metastases or fracture is made in the post-mortem records, the presumption in favour of their freedom from extensive new growth is so considerable as almost to amount to a certainty.

Spontaneous fractures have been reckoned as indicating metastases at the point of fracture, whether the existence of local growth has been specially mentioned in the records or not.

The following table shews the relative frequency of deposits in the various bones of the skeleton :—

TABLE I.—Showing the Frequency of Cancerous Deposit, or Spontaneous Fracture, in 329 Cases of Mammary Cancer at the Middlesex Hospital, 1872–1901.

	Bone.	Number of Cases.	Percentage of Total.
Bones lying wholly or partially within the area liable to subcutaneous nodules.	Sternum	30	9
	Ribs	28	8
	Clavicle	5	1·5
	Spine	12	3·6
	Cranial Bones	9	2·7
	Scapula*	1	·3
	Femur	14	4·2
	Os innominatum*	0	0
	Humerus	9	2·7
Bones lying beyond the area liable to subcutaneous nodules.	Radius	0	0
	Ulna	0	0
	Tibia	1†	·3
	Fibula	0	0
	Patella	1†	·3
	Bones of Hand	1	·3
	Bones of Foot	0	0

Making full allowance for the fallacies inherent in this table, and the errors of omission relating to the bones not liable to spontaneous fracture, it will be found to indicate certain general laws.

(1) *The liability of a Bone to Cancerous Metastases increases with its proximity to the site of Primary Growth.*

Thus, the sternum and ribs are affected in about the same number of cases, and much more frequently than any of the other bones. The spine, femur, humerus, and cranial bones come next, the clavicle apparently forming an exception to the general rule.

* This bone, owing to its shape, is not much liable to spontaneous fracture, and rarely comes under observation at an autopsy (see page 31).

† Knee ankylosed, femur affected in its whole length, with extension of growth to patella and head of tibia (see page 40).

(2) *The Bones distal to the Knee and Elbow escape Cancerous Invasion, except in the rarest instances.*

Among the seventy-three cases of bone deposit or fracture there are one real and one apparent exception to this rule. These two cases will be dealt with in detail later on.

If bone deposits take their origin from particles lodging in the peripheral blood-vessels they can best be studied in the limbs, the regions which appear most liable to embolism. If, on the contrary, the view be accepted that bone deposits are incidents in the centrifugal spread of the cancer by continuity, it is equally in the limbs that clear evidence on the point is likely to be obtained. For this reason metastases in the bones of the trunk may be ignored, and attention will be concentrated on the long bones of the limbs.

(*a*) Secondary Deposits in the Femur.

Out of 329 cases there are recorded nine in which one or both femora were the seat of definite deposits, with or without fracture, and five others in which spontaneous fracture alone is said to have occurred. In twelve of the fourteen cases, there was fracture of one or both femora; in four cases the fracture was bilateral.

In every case where the deposit was local or the fracture single, the pathological condition was present in the upper third of the bone, most often a little (about two inches) below the base of the great trochanter.

This statement is based on eleven of the fourteen cases, and the apparently exclusive preference of early cancerous growth for this particular part of the bone is a striking fact. The point of election for spontaneous fracture in breast-cancer does not coincide with the usual positions of senile fracture of the femur, which is across the neck, nor with the point of entry of the nutrient artery.

There are indications that the base of the great trochanter is the usual point of invasion of the femur, but that, owing to the thickness of the bone at this level, actual fracture generally occurs rather lower down. Thus in Case XII.* there was

* For table of cases of secondary cancer of the femur and humerus, see Archives of the Middlesex Hospital, Vol. iii.

fracture of the right femur "through its upper third." The new growth was chiefly confined to the upper fragment, involving the great trochanter, *which was largely destroyed*, and the shaft just below.

Again, in Case VII., at the junction of the shaft with the great trochanter, there was a mass of cancer the size of a man's fist. The bone was fractured.

The right femur in Case XI. afforded similar evidence. There was new growth over the great trochanter, and again about 3½ inches below this.

Even in cases where the infiltration of the femur is very extensive, or has extended along its whole length, the indications that the bone was originally attacked near the upper end are often quite clear. Thus in Case XIII. the right femur was infiltrated in its upper two thirds, the lower third having escaped. In Case III. the right femur was distorted and in great part replaced by growth, and only in its lower third was the outline of the bone traceable.

It thus appears that secondary cancerous deposit in the femur always commences in the upper third, and never in the distal portion of the bone. There is strong evidence that the great trochanter is the point of first invasion.

Of eight cases showing unilateral fracture of the femur, the fracture was on the same side as the primary growth in six cases, and on the opposite side in only two cases.

(*b*) Secondary Deposits in the Humerus.

Among the 329 cases dealt with there were six in which one or both humeri were the seat of deposits. In five of these cases attention was directed to the bone by the presence of fracture. In four other cases there was fracture without any definite proof of the presence of growth, making ten in all. In two of these ten cases the fracture was bilateral.

Of the eight separate bones in which fracture occurred, and in which the exact site of the break is recorded, it was found just at the middle of the bone in four instances, and through the lower third in the remaining four. Fracture therefore occurs within the limits of the lower half of the

bone, and the seat of election is the mid-point of the bone at the deltoid insertion.

Cancerous deposit in the humerus is much more frequent than would appear from post-mortem records.

Snow* records eight cases of microscopical infiltration of the bone in an unselected series of twelve cases of cancer of the breast examined by him. The same observer has directed attention to a thickening of the upper epiphysial end of the humerus, sometimes to be felt on the side of the primary growth, which he regards as cancerous.

A cancerous humerus seems to be less liable to spontaneous fracture than the femur, partly because it carries less weight, partly, no doubt, because it is often supported by a firm œdema of the arm, and is also bound to the side by contraction of the axillary growth. Hence post-mortem statistics probably underestimate the frequency of deposit in the humerus, especially as the humerus is liable to a risk not shared by the femur, viz., direct invasion by a mass of axillary growth. Hence also fracture of the humerus is more frequent on the side opposite to the primary growth.

The evidence goes to show that, as a rule, it is not direct extension of the axillary growth that leads to spontaneous fracture. *Apparently the humerus is usually invaded at its mid-point—the deltoid insertion—from which point the growth spreads both upwards and downwards along the medullary canal.* The relative thinness of the lower half of the bone, and the smaller amount of protection it receives, account sufficiently for the incidence of spontaneous fractures on this portion of the bone.

(*c*) Secondary Deposits in Long Bones of the Limbs other than the Humerus and Femur.

These may be very briefly dismissed. In one case the scapula was involved; in another case the head of the tibia was invaded by extension from advanced growth of the femur, apparently by way of an ankylosed knee-joint. In another case there were spontaneous fractures of three metacarpal bones. Both these latter cases will be referred to again.

* "The Insidious Marrow Lesions in Mammary Carcinoma," Snow. (*British Medical Journal*, March 12th, 1892, p. 548.)

The absence of records of spontaneous fracture in the distal bones shows that their escape from cancerous invasion is real and not merely apparent.

The Pathogenesis of Bone Metastases.

There is a consensus of opinion that bone metastases in carcinoma mammæ, and in carcinoma generally, are due to transference of particles of the primary growth by way of the blood stream.

A consideration of the evidence seems to show that the conclusion is an erroneous one, and that, like subcutaneous nodules, bone deposits are usually secondary results of far-extending growth of cancer along the deep fascial lymphatic plexus. Whether the same holds good for cancer of other regions than the breast is not now the subject of discussion.

These two hypotheses may now be considered separately.

A.—*Are Bone Metastases due to Blood-infection?*

(*a*) There is one fact with reference to secondary growths of the femur and humerus which seems at first sight strongly to suggest their origin from emboli carried along the blood-vessels. Bone deposits in an early stage involve the upper third of the femur, but the lower half of the humerus. They thus occur mostly in that district of the bone towards which the nutrient artery of the shaft is directed.

More closely examined, this contention loses much of its force. The seat of election for cancer of the femur is the great trochanter; of the humerus, it is at the deltoid insertion. One would rather imagine, if the process were embolic, that the seat of election in the femur should be in the neck, near the epiphysial line, and not at a point distinctly lower down. Again, in the humerus, where the nutrient artery enters below the mid-point of the bone, the line at which fracture is most often found—the deltoid insertion—lies *above* the nutrient foramen and not below it, as would be required on the embolic view.

(*b*) If bone deposits are disseminated by the blood stream it seems reasonable to argue that the cases in which they

occur should show pulmonary metastases with especial frequency.

As a matter of fact, deposits in the lungs were only present in 24 per cent. of the 37 cases showing extensive bone deposits or spontaneous fractures, while pulmonary metastases are recorded in 26 per cent. of the entire series of 329 cases. On the other hand, deposits in the liver were present in 46 per cent. of the cases showing bone cancer, while they occur in only 42 per cent. of all cases.

These figures on the whole offer no support to the current theory that bone metastases are produced by way of the blood. For there is no marked difference in the incidence of visceral metastases between the cases which show bone deposits and the cases in which they are absent.

It is true that M. B. Schmidt (see Chapter I) has recently shown how occasionally small cancerous emboli lodged in the lungs may grow along the capillaries and small pulmonary veins, and may thus give rise to systemic embolism without producing any macroscopic changes in the lung. But these cases must be somewhat exceptional, and cannot entirely invalidate the preceding argument.

(*c*) But the weightiest argument against blood infection as a cause of bone deposits lies in the entire escape from metastases of the tibia and fibula, the radius and ulna, the bones of the hand and foot. These bones are just as liable to embolism as the femur or the humerus—probably more so, on account of their greater nearness to the periphery of the circulation—and yet metastases in them are of the rarest occurrence.

In the Middlesex Hospital Archives, Dr. Reginald Gladstone has described a case of carcinoma of the left breast in which there were osseous metastases in the vault of the skull, the right clavicle, some of the ribs, both innominate, and both thigh bones.* Dr. Gladstone believed that the cancerous invasion of the skull, which practically coincided in area with the distribution of the middle meningeal arteries, arose from cancerous embolism of these vessels. But in spite

* R. Gladstone, "A Case of Secondary Carcinomatous Deposit in Bone, with especial reference to the Vascular Supply of the Metastases" (Archives of the Middlesex Hospital, Vol. iii., 1904).

of a very careful and complete microscopical examination, he does not record the detection of any cancerous embolus.

It appears to be more probable that the skull was invaded by the extension of permeation along the lymphatic vessels which may be presumed to accompany the middle meningeal artery. It is well known that lymphatic vessels, as well as veins, frequently accompany an artery and have an almost identical distribution. And in the case in question the carotid vessels and large nerves were firmly embedded in a dense fibrous growth which extended upwards into the parotid and submaxillary regions. Evidently therefore a mass of growth had reached the immediate vicinity of the *foramen spinosum*, through which permeation might readily carry it along the lymphatics into the interior of the skull.

B.—*Are Bone Metastases a Secondary Result of Centrifugal Growth along the Deep Fascial Lymphatic Plexus?*

The fact that the bones nearest the primary growth are more frequently, and those farthest from it most rarely, the seat of metastases, might seem at first sight to suggest that there is actual continuity of growth along the skeleton from the primary cancer outwards to the distal extremities. But the breaking up of the skeleton into distinct segments separated by joints makes such a hypothesis untenable. And evidence has already been adduced that the centrifugal spread of breast-cancer takes place primarily along the deep fascia. As in the case of subcutaneous nodules, the irregular incidence of bone metastases within a definite area marks them as casual secondary results of the fascial infection. Such a view accounts satisfactorily for the progressively increasing immunity of the more distal bones.

Since there is no suggestion that the growth spreads primarily along the skeleton by continuity, it is not to be expected necessarily that growth will always begin at the proximal end of each bone and extend along it to the distal end. Indeed, a moment's reflection convinces one that such an event is most unlikely. For if the humerus and femur are invaded from the lymphatic plexus of the deep fascia, *the*

first attack should be directed on that point at which the bone lies nearest to the deep fascial lymphatics, and therefore on that point at which the bone comes nearest to the cutaneous surface. Moreover, in the case where a bone is provided with two or more subcutaneous areas, the seat of first attack, according to the view of centrifugal spread, must be that area which is nearest to the trunk. Thus, on the hypothesis we are discussing, the point of invasion of the femur should be, and in point of fact is, the base of the great trochanter and the adjoining part of the linea aspera. The point of invasion of the humerus should be, and actually is, relatively much lower down, at the deltoid insertion, since the whole of the upper half of the humerus is well clothed by muscles.

Centrifugal extension, therefore, explains the peculiar seats of election of spontaneous fractures of the humerus and femur in a far more satisfactory manner than embolic infection by way of the blood stream.

There is no need to insist further on the explanation it affords of the immunity of the bones distal to the knee and to the elbow. These bones escape simply because the patient dies almost invariably before growth has spread along the deep fascia far enough to reach them.

Coincidence of the Areas liable to Bone Metastases and to Subcutaneous Nodules.

It will not have escaped notice that *bone deposits only occur in bones which lie partially or wholly within the area liable to subcutaneous nodules.*

Among the seventy-three cases of bone deposit or fracture with which this chapter deals, there are two which offer apparent exceptions to this rule.

(1) In one case there were bone deposits in the left humerus, both femora, the right tibia, and the right patella. The right femur was infiltrated in its whole length. *The right knee-joint was ankylosed*, and there was growth at the back of the patella and in the head of the tibia. There was osteo-arthritis of the left knee-joint.

Owing to the osteo-arthritic ankylosis of the knee-joint the tibia and patella were practically continuous with the femur. So far, therefore, from weakening the evidence for centrifugal spread, this case strengthens it.

(2) In another case the body presented a deformed appearance, the limbs being much distorted and the spine curved. Both humeri were fractured, the left at the mid-shaft and the right at the lower third. The left clavicle and the left femur were fractured, the latter two inches below the great trochanter. All these fractures had united. The third, fourth, and fifth right metacarpals showed un-united fracture.

This case forms the only real exception to the rule just stated. It is quite conceivable that in rare cases the patient may survive until centrifugal extension has involved every bone in the body, and this case seems to be an approximation to that condition. It is worthy of note that the patient had considerable powers of resistance and repair, as is shown by the fact that all the proximate fractures had united. On the other hand the distal fractures, though they occurred in bones in which quick repair is usual, were un-united. On the centrifugal hypothesis this non-union of the metacarpal fractures is easily understood, because the growth could only have reached them at a very late stage of the disease. A close perusal of these cases shows that with this single inconclusive exception the rule enunciated at the beginning of this paragraph appears to be nearly absolute.* *Metastases do not occur in bones lying entirely outside the area liable to subcutaneous nodules.* Nevertheless it is not quite true that the areas of subcutaneous nodules and of bone metastases absolutely coincide. Whenever a long bone such as the femur is invaded, the growth spreads rapidly along the medullary canal, and soon involves the whole length of the bone. Hence the only areas free from bone invasion are the parts distal to the knee and to the elbow.

The fact that bone metastases do not occur in bones lying outside the area liable to subcutaneous nodules may be

* Mr. J. R. Lunn, Medical Superintendent of the Marylebone Infirmary, has lately informed me of a case of breast-cancer under his care with a secondary deposit in the ulna. I do not deny that in rare cases bone-deposits may be the result of arterial or capillary cancerous embolism.

emphasized by comparing an extreme instance of each condition :—

Bone Deposits.

Plaster-cast No. 673, St. Thomas's Hospital Museum.—The body of a woman who died from scirrhus of the right breast. The skeleton has undergone great distortion. The sternum and ribs have sunk until the former almost appears to touch the vertebral column, the whole thorax being flattened out transversely. The pelvis exhibits a precisely similar modification. The right humerus and both femora have undergone fracture. Right humerus fractured near deltoid insertion, right femur just below the middle, left femur higher up. (*See* FIG. 8, which is a photograph taken from the cast of this case.)

Subcutaneous Nodules.

Dr. Rolleston's Case, Clinical Society's Transactions, 1901, p. 206.—Cancer of left breast. Subcutaneous nodules distributed irregularly over the whole surface of the body except the distal portions of the limbs. The nodules extend down the left arm below its mid-point, down the right arm to the level of the anterior axillary fold. They have extended to both groins, reaching on the right side a hand's breadth below Poupart's ligament. Fracture of the left femur occurred in a late stage of the case. (*See* FIG. 5.)

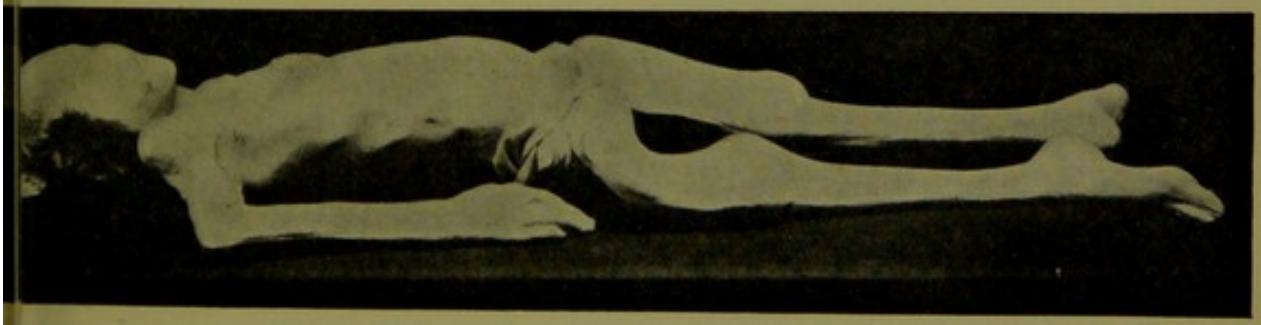


FIG. 8.—Photograph of Plaster Model, No. 673, St. Thomas's Hospital Museum by kind permission of Mr. Shattock.—The body of a woman who died of Scirrhus of the Right Breast. The figure is inserted to illustrate the immunity of the bones distal to the knee and elbow, even in an advanced stage of Secondary Bone Cancer.

Fig. 9 indicates the areas liable to subcutaneous nodules and to bone metastases respectively.

The existence of a relationship between bone deposits and subcutaneous nodules is further brought out by their frequent association in the same case. Subcutaneous nodules were present in 22 per cent. of the whole series of 329 cases, while they occurred in 27 per cent. of the 73 cases with bone deposits, and in no fewer than 40 per cent. of the 20 cases which showed extensive bone deposits, as indicated by metastases or fractures in the femur or the cranial bones.

In the preceding pages a considerable weight of evidence has been brought forward to show that both subcutaneous

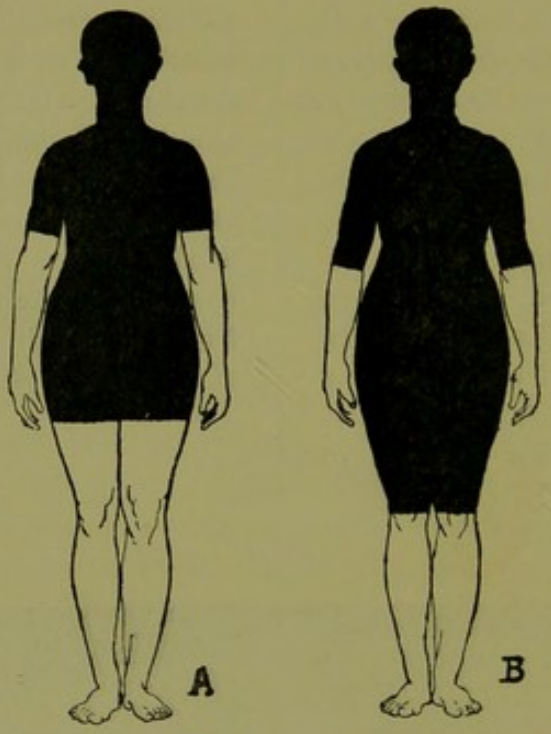


FIG. 9.—Diagrams showing the maximal distribution areas of subcutaneous nodules and of metastases in bone in cases of mammary carcinoma. The black area in A is the area liable to subcutaneous nodules, that in B is the area within which bone metastases occur.

nodules and bone metastases result from far-reaching centrifugal growth of cancer in the parietes, but the question in which layer of the parietes cancer primarily spreads still remains to be settled. The problem can be definitely solved only by the microscope (see Chapter IV.), but it is possible from clinical evidence to obtain indications whether centrifugal growth takes place along the skin and subcutaneous tissue or along the deep fascia.

The problem is one of immense importance for the future operative treatment of cancer of the breast. Removal of the skin has reached already its furthest possible limits, and it is therefore not surprising if surgeons who hold that cancer spreads along the skin believe that no great improvement upon present results is likely to be attained. Prof. Halsted, who invariably removes so much skin that he is unable to sew up the wound, says: "When operating for cancer of the breast we cannot be responsible for undiscoverable metastases in the skin. For the principal growth, the axilla, the pectoral muscles, and the supra-clavicular region—in other words, for the scar in its fullest sense—we should hold ourselves responsible, but for the eradication of the so-called lenticular and apparently discrete metastases of the skin we have no guide. One might literally flay the patient's chest and side, only to find, weeks or months later, one or more cancer nodules in the skin of the neck, or the back, or abdomen."

Prof. Cheyne,* too, says: "I think that we may now form a fairly final judgment with regard to the treatment of cancer of the breast by operation."

But if the accepted theory of the spread of cancer is erroneous—if breast-cancer instead of spreading along the skin spreads along the deep fascia, and only here and there blossoms outwards into skin nodules—the results of operation are certainly capable of improvement, for it is possible to remove the deep fascia over a wider area than has ever yet been practised.

In my opinion a most important indication in this direction is afforded by a comparison of the operative methods and results of Profs. Cheyne and Halsted. Both operators practise a wide removal of skin; but whereas Cheyne generally succeeds in sewing up the wound, Halsted has usually to resort to skin grafting. It may therefore be assumed with certainty that the American surgeon removes more skin than does his English colleague.

Cheyne lays special stress on the undermining of the skin all round the incision, while Halsted, on the contrary, nowhere refers to the undermining of the skin so as to secure removal of an area of deep fascia wider than that

* *Lancet*, March 12th, 1904.

of the skin removed. In Halsted's operation the skin incisions "are carried at once and everywhere through the fat." Then in removing the breast: "the whole mass, skin, breast, areolar tissue and fat, *circumscribed by the original skin incision* (italics not in the original), is raised up with some force, to put the submuscular fascia on the stretch as it is stripped from the thorax close to the ribs and pectoralis minor."

The differences in other respects between the two operators are unimportant for my present purpose. What I would lay stress upon is that while Halsted removes more skin than Cheyne, Cheyne carries out a far freer ablation of the deep fascia than Halsted.

A study of the results of the two operators with regard to local recurrence should therefore give valuable indications. If cancer spreads centrifugally along the skin, Cheyne's wide removal of the deep fascia is evidently a vain precaution, and Halsted's extensive removal of skin is correct. If, on the contrary, cancer spreads along the deep fascia and only secondarily invades the skin, Halsted's free removal of skin will be invalidated by his failure to remove the more widely infected deep fascia around his wound.

The records of local recurrence in the two sets of cases will be found summarised in the table on the following page.

This table shows that the practice of removing a very wide area of deep fascia and a less wide area of skin gives better results than the removal of less fascia and more skin.

Taking skin recurrences only, Halsted gets 16 per cent. and Cheyne 6·5 per cent. If the latter's three cases of local recurrence of unknown position be all counted as skin recurrences his percentage is raised to 11 per cent., but even then the difference is still one in favour of the operation with wide removal of deep fascia.

This table shows that the operator who removes the smaller area of skin, yet has a lower percentage of skin recurrences, a result which is unintelligible if cancer spreads along the skin. The operator who removes the smaller area of deep fascia has a higher percentage of skin recurrences, in spite of his wider removal of skin, because growth

TABLE II.

SHOWING THE COMPARATIVE RESULTS OF VERY WIDE REMOVAL (*a*) OF SKIN, (*b*) OF DEEP FASCIA, IN BREAST CANCER.

Operator.	No. of Cases.	Practice as regards removing		Percentage of Successes.	Percentage of External Recurrences.	Situation of External Recurrences.		
		Skin.	Deep Fascia.			Local Recurrence, Position unknown.	Pectoral Muscles or Ribs.	**Surrounding Skin.**
Halsted	50	very wide removal.	removal coterminous with that of skin except towards axilla, where it is greater.	41 per cent.	22 per cent.	...	3 cases = 6 per cent.	**8 cases = 16 per cent.**
Watson Cheyne	61, 1st series	wide removal.	very wide removal.	upwards of 50 per cent.	18 per cent.	3 cases = 4·9 per cent.	4 cases = 6·5 per cent.	**4 cases = 6·5 per cent.**

subsequently extends to the skin from the infected area of the deep fascia which has been left behind. The cancer appears to be spreading primarily along the deep fascia. This conclusion is strengthened by a study of the site of the skin recurrences, which usually appear immediately beyond the edge of the area of deep fascia removed. Cheyne mentions the site of recurrence in two cases. In one of these a skin nodule developed near the angle of the scapula, in the other at the edge of the latissimus dorsi. In four of Halsted's cases the recurrence was at the outer, or lower and outer, side of the scar, and in one over the opposite breast.

Thus, although Cheyne removes less skin than Halsted, yet the skin recurrences in his cases are situated further away from the site of primary growth.

And finally, a glance at Halsted's sketch of the parts removed by his operation shows that his removal of the deep fascia is at its minimum along the inner, and along the lower and outer sides of the breast, situations at which skin nodules developed in at least five of his eight cases of cutaneous recurrence.

CHAPTER III.

THE ROUTES OF LYMPHATIC DISSEMINATION IN THE PARIETES.

The Lymphatic Anatomy of the Parietes.

BEFORE proceeding further it is necessary to review the lymphatic anatomy of the parietes, which to a large extent determines the mode of spread of cancer in the parietal tissues. The lymphatics of the skin originate in the papillæ, and communicate in the superficial layer of the dermis to form the sub-papillary plexus. From this plexus vessels arise, which pierce the dermis at right angles to the surface, and pass along the fibrous septa of the subcutaneous fat to empty themselves into the main parietal lymphatic plexus, which lies upon or just over the deep fascia. According to Sappey, the lymphatics which drain the skin do not form at the deep aspect of the dermis the deep cutaneous plexus described by Arnold, and since accepted by many writers on his authority.

Sappey * thus describes the lymphatics of the dermis:—

> "If one divides the dermis into three layers—a superficial, a middle, and a deep—it is noticeable that over the greater part of the surface of the skin it (the sub-papillary plexus) terminates at the union of the first with the second. In some regions, as the palm and the sole, it descends even into the middle layer, but never beyond this point. In the deeper half of the dermis one sees only trunks starting from the sub-papillary plexus, which dip down vertically, without anastomosing between themselves, and without forming on the deep aspect of the skin the second plexus which so many authors have admitted without ever having seen it, and which Arnold has had the audacity to represent, *en le composant de toutes pièces.*"

* Sappey, "Vaisseaux Lymphatiques," page 17.

Personally, although I have examined a large number of sections in which both the sub-papillary and the fascial plexuses were mapped out by cancerous epithelium lying within them, I have never been able to obtain any similar evidence of the existence of the "deep cutaneous plexus."

Besides the small tributaries which dip down vertically into the fascial plexus from the surface of the body, there are running upwards to the deep aspect of the fascial plexus numerous vessels by means of which it communicates with the lymphatics of the subjacent tissues. I have frequently observed such vessels passing to the deep fascia from the muscles, and the special liability of some of the subcutaneous areas of the skeleton to cancer appears to show that the fascial plexus anastomoses in a similar way with the periosteal lymphatics wherever they approach the surface.

It is often stated on Sappey's authority that the lymphatics of the breast, which have been so fully described by Stiles* and other authors, drain largely into the subareolar plexus which lies superficially upon the mammæ just beneath the skin of the areola, and that from this plexus trunks arise which run direct to the axillary glands without entering into relation with the fascial plexus. If this is really the case the lymphatic arrangements of the breast are quite exceptional, for all the other cutaneous appendages such as the sweat glands drain into the fascial lymphatic plexus, and the breast is after all only a highly-developed group of sebaceous glands.

On this, as on other debatable questions of lymphatic anatomy, the study of cancer is capable of throwing light. The opposite breast and opposite axillary glands are frequently invaded in the later stages of breast cancer. If the infection spreads to the opposite side by way of the subareolar plexus and the lymphatics of the skin, it is obvious that it will reach the opposite subareolar plexus and the surface of the opposite breast before it reaches the opposite axillary glands, and that invasion of the opposite breast, superficial and therefore appreciable, will precede in point of time enlargement of the opposite axillary glands. But in twenty-five cases I have collected showing cancer

* Stiles, "Trans. Edin. Med.-Chir. Soc.," Vol. xi., pages 37–70.

of the opposite axillary glands, the opposite breast still remained normal in nine cases. It is thus highly probable that, as Stiles first pointed out, invasion of the opposite breast is secondary to invasion of the fascial lymphatic plexus beneath the breast, from which embolic particles are swept to the opposite axillary glands before the invasion of the deep surface of the breast has had time to become clinically obvious. If this be the real sequence of events the lymphatics of the breast, like other cutaneous lymphatics, must drain chiefly into the deep fascial (retro-mammary or pectoral) lymphatic plexus, and must thence pass indirectly to the axillary glands, a conclusion which accords with other known facts of dissemination, and especially with the work of Heidenhain (page 51).

The Fascial Lymphatic Plexus.

The lymphatic plexus of the pectoral fascia is often spoken of as if it were an anatomical entity. It is in reality merely a conventional sub-division of the deep fascial lymphatic plexus, whose network of intercommunicating channels invests the entire body. This great plexus is divisible by the median plane of the body, and by two horizontal planes passing through the clavicles and through the umbilicus respectively, into six catchment areas, three on either side, draining as the case may be into the cervical, the axillary, or the inguinal glands. Within each area a special set of trunk lymphatics arises from the plexus and converges on the corresponding set of glands. The line, or rather zone, separating any two adjacent areas, may be called the lymphatic water-parting, and is anatomically a zone of narrow tortuous channels nowhere traversed by trunk lymphatics, a region consequently where the lymph stream is at its feeblest, and where even very fine particles are liable to be arrested. (See Fig. 10.)

The general idea then, which we have obtained of the parietal lymphatic system is that of a vast horizontal network of fine channels, co-extensive with the surface of the body, and receiving above numberless fine vertical tributaries, which convey to it the lymph from the skin and its appendages. Among the latter we must include the breast. On its deep aspect the plexus receives tributaries from the subjacent

tissues. From this great plexus, which lies in the subcutaneous fat upon the deep fascia, the lymph is conveyed by six sets of lymphatic trunks, each draining a definite area, to the cervical, the axillary, or the inguinal glands.

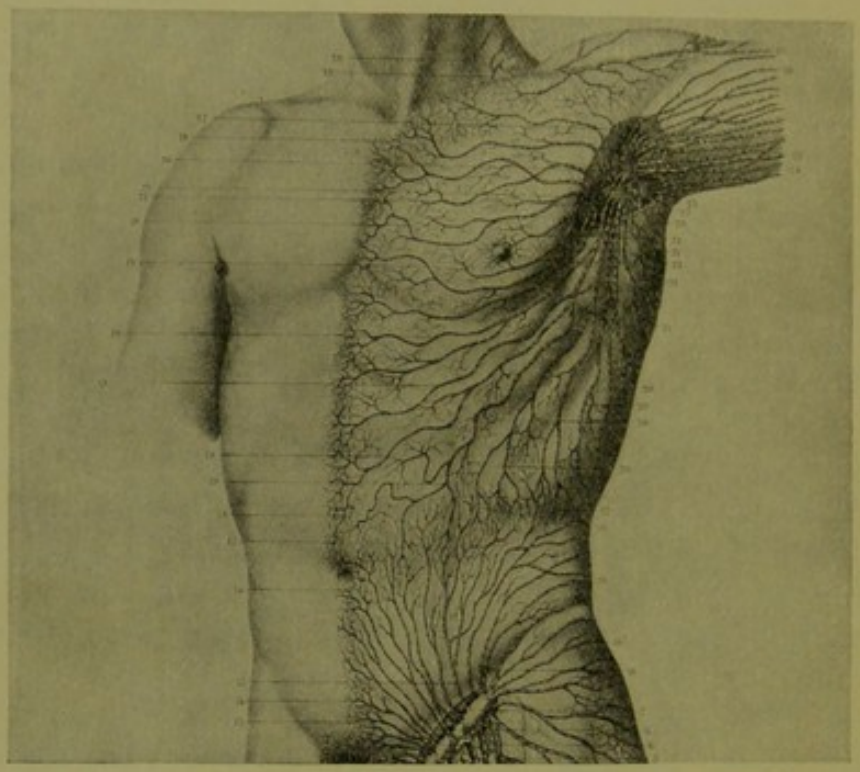


FIG. 10.—From a plate in Sappey's *Vaisseaux Lymphatiques*, showing the lymphatic plexus (fascial lymphatic plexus), which lies in the deepest layer of the subcutaneous fat, and forms the main highway for permeation in breast-cancer. Numerous trunks are seen arising from the plexus, and passing to the axillary or the inguinal glands. Along these trunks embolic invasion of the axillary glands occurs, the trunks themselves escaping permeation until a late stage. The fine meshwork of vessels constituting the fascial plexus is only partially indicated in this figure, so that the trunk-lymphatics are made to appear unduly prominent.

We are now in a position to trace the advance of a carcinoma along the ramifications of the great parietal lymphatic plexus. The subject may be divided as follows:—

(1) Dissemination within the limits of the breast.
(2) Invasion of the underlying pectoral fascia.
(3) Embolism of the axillary glands and invasion of other lymph glands.
(4) Retrograde embolism produced by a reflux lymph stream.
(5) Centrifugal lymphatic permeation.

Dissemination within the limits of the Breast.

Much of the literature of breast-cancer centres on this subject. Since I can add nothing to the valuable and well-known work of Langhans, Heidenhain, Stiles, and many other authors on this subject, I do not propose to deal with it. Langhans was the first to observe that the small lymphatics of the breast are invaded early and widely, far beyond the infiltrating edge of the primary growth. It has remained, however, still uncertain whether this lymphatic invasion is embolic, or proceeds by continuous growth along the vessels. Stiles*, who examined over one hundred breasts removed by operation, shared the embolic view of Langhans. But my own investigations in the extra-mammary tissues, where the conditions of observation are perhaps more favourable, show continuous growth of cancer along the lymphatics (see Chapter IV.), and it seems unlikely that the predominant mode of spread within the breast is by a different method.

The division of opinion on this subject appears mainly due to a non-recognition of the fact that lymphatics along which cancer cells have pushed their way, subsequently undergo obliteration, leaving isolated nodules of growth here and there where the process of obliteration has failed (see Chapter IV.).

Extension of Growth to the Pectoral Fascia.

Heidenhain,† in twelve out of eighteen cases examined, found cancerous lymphatics running from the breast to the pectoral fascia. His observations showed that the cancer generally advanced along these vessels and along those of the pectoral lymphatic plexus by a process of continuous growth, less often by embolism.

It is an important fact that cancerous lymphatics may be found in the pectoral fascia before the growth has become adherent to the muscle, an observation I was able to confirm in a recent case. Thus in an early stage, prior to adhesion to

* Stiles, "On the Dissemination of Cancer of the Breast," *Brit. Med. Journal*, 1899, Vol. i., p. 1452.

† Heidenhain, "Ueber die Ursachen der localen Krebsrecidive nach Amputatio Mammae," Arch. fur klin. Chirurg., 1889, p. 97.

the skin, and even before adhesion to the pectoral fascia, an area of the deep fascial (pectoral) lymphatic plexus which underlies the growth, shows cancer-filled lymphatics. I shall be able to show that the parietal metastases of breast-cancer are especially frequent and widespread, not on account of any special cancerous proclivity of the skin in the subjects of breast-cancer, but because of the intimate connection which Heidenhain proved to exist between the lymphatics of the breast and those of the great fascial plexus.

Embolism of the Axillary Glands.

Embolic invasion of the axillary glands almost invariably occurs in an early stage of breast-cancer. In the first stage of gland invasion a few cancer cells are seen lying in the sub-capsular lymph sinus at the point of entry of the afferent lymphatics, along which the cancer cells have been swept by the lymph stream (Stiles). The cancer cells slowly penetrate into the interior of the lymph-gland by a process of actual growth through the lymph spaces of the gland. After a considerable lapse of time they may in this way reach the efferent lymphatics, along which they pass, either embolically or by actual growth, to the next set of glands. Moreover, when the cancer cells have succeeded in penetrating the fibrous capsule of the lymphatic gland, they infiltrate the surrounding structures, and the gland in consequence loses its mobility and becomes a focus of local infection.

The lymph glands, though ultimately they may become infective foci, for a long time delay the progress of any cancer cells which reach them. Not only do they act as mechanical filters, but there is evidence that for a time at least they exert a destructive action on cancer cells which reach them, and that they only succumb to the invasion after a prolonged resistance.

The clinical prominence of enlargement of the lymphatic glands in cancer has caused undue importance to be attached to their invasion, which is generally assumed to be an essential step in the process of dissemination. It is therefore important to emphasize the fact that widespread dissemina-

tion may occur, as in the two following cases, without any permanently successful cancerous invasion of the lymphatic glands. In both cases, no doubt, the abdomen was invaded through the epigastric parietes (see Chapter V.).

Case 1.—Autopsy No. 215, The Middlesex Hospital, 1879. The patient, aged 58, had a cancer of the left breast. Eighteen months after the tumour appeared zinc chloride paste was applied; the patient died three years later. At the necropsy there was a large crateriform ulceration in the situation of the left breast, without outlying knots, and without infection of lymphatic glands. In the cirrhosed liver were a few nodules of cancer.

Case 2.—Autopsy No. 380, Guy's Hospital, 1891. The patient, aged 48, had a cancer of the right breast. At the necropsy there was found a hard growth adherent to the pectoral muscle, and very close to but not involving the skin. The axillary glands were normal. The liver weighed 70 ounces, and showed numerous white capsular nodules, and many small white nodules in its interior. No operation had been performed.

Embolism of the axillary glands is probably always secondary to the growth of cancer along the meshes of the pectoral lymphatic plexus which Heidenhain observed. As soon as cancer cells intrude from the smaller vessels of the fascial plexus into a trunk lymphatic, they are swept by the stream to the axillary glands. After long delay they penetrate these glands and the supra-clavicular glands, and so attain the blood stream.

The route we have been tracing is usually regarded as the main avenue of dissemination. So no doubt it might be, but for one factor—the destructive action of the blood on cancerous epithelium, which was demonstrated by Schmidt. The peculiarities of metastatic distribution (Chapters II. and VI.) are in themselves sufficient to show that cancer cells which gain access to the blood are usually reduced to impotence.

Retrograde Lymphatic Embolism.

There is, however, another route by which dissemination might occur. As soon as the lymphatic glands are obstructed by growth a reflux lymph-stream must pass across the middle line to the opposite axillary glands, upwards to the cervical or downwards to the inguinal glands.

Very great stress has by some authors been laid on this factor in dissemination. But retrograde embolism cannot take place to any extent in trunk lymphatics on account of the valves which are present in them. Moreover, as Fig. 10 showed, towards the periphery of each lymphatic area the trunks break up into fine plexuses. Clearly, therefore, the reflux lymph stream cannot carry cancer cells out of the lymphatic area in which the primary growth arose, and into adjoining areas, unless it is sufficiently forcible to drive the cancer cells through networks of small lymphatic vessels. And the feeble lymph-stream of the lymphatic plexuses is inadequate for this task, for as will appear in Chapter IV., *no outlying embolic foci can be found outside the microscopic parietal growing edge of a breast-cancer.* And the opposite axillary glands, the opposite breast, or the inguinal glands, are never found to become cancerous early in the case, as should occasionally happen if cancer-cells can reach them embolically from other lymphatic areas.

Cases showing Invasion of the Axillary Glands on the side opposite to the Primary Growth.

Invasion of the opposite axillary glands is not a very uncommon event; it occurs, however, only in a very late state, as is shown by the fact that it was only found once in the Guy's Hospital (or early) series of cases, as against twenty-four times in the Middlesex Hospital (or late) series.*

Thus in the whole number of 422 cases it was found in 6 per cent.; in the early cases in 1 per cent.; and in the late cases in 7 per cent.

It probably indicates that permeation has extended well over the middle line, and that cancer-cells have thus penetrated to the trunk lymphatics which drain into the opposite axillary glands.

The frequency of invasion of these glands is probably much greater than would appear from post-mortem records.

* The facts on which this distinction between early and late cases is based will be found stated on page 116.

Infection of the Opposite Breast.

This was found in 66 of 422 cases, i.e., 15 per cent. It was present in 18 per cent. of the Middlesex Hospital (late) cases, and in only 5 per cent. of the Guy's Hospital (early) cases. It is therefore a late event in the course of breast-cancer.

The lateness of occurrence of infection of the opposite breast and opposite axillary glands is one of the best proofs that cancer cells cannot be transmitted through lymphatic plexuses by the lymph stream, but must actually grow through them by a process of permeation.

Infection of the Inguinal Glands.

The inguinal glands are recorded as showing secondary deposit in six (1·8 per cent.) of the Middlesex Hospital, and in one (1 per cent.) of the Guy's Hospital cases.

Infection of the abdominal cavity is not a necessary precursor of growth in the inguinal glands, for it was entirely absent in two cases, and in a third there was only a single nodule within the abdomen. On the other hand, in two cases there were very advanced secondary deposits in the abdomen, to which apparently the enlarged inguinal glands were secondary.

These two cases excepted, the remaining five showed marked evidence of fascial permeation (a process shortly to be dealt with) either in the form of subcutaneous nodules (four cases), or of cancer *en cuirasse* (one case). Fifty-seven per cent. of cases where the inguinal glands were cancerous showed skin nodules in addition, while the latter only occur in eighteen per cent. of all cases.

I believe that breast-cancer usually infects the inguinal glands by growing along the small vessels of the deep fascial lymphatic plexus of the anterior abdominal wall. As soon as permeation has extended downwards to the level of the umbilicus, embolic invasion of the inguinal glands is possible along the tributary trunk lymphatics which course downwards to the inguinal glands (Fig. 10).

Infection of the Supra-clavicular Glands.

Under this heading there are included all cases where either the supra-clavicular or the cervical glands are recorded

as being infected. Deposits were found in these glands in 61 (18 per cent.) of the 329 Middlesex Hospital cases, and in 12 (13 per cent.) of the 93 Guy's Hospital cases, or in 17 per cent. of the whole number of cases. Halsted has shown that these glands often contain cancerous foci when to the naked eye they appear normal.

As a rule these glands are palpably enlarged only on the side of the primary growth, but in three cases the glands of the opposite side only were infected, and in four cases the process was bilateral. In one case the enlarged glands had ulcerated.

It appeared possible that infection of the supra-clavicular glands might occur, independently of infection of the axillary glands, as a result of fascial permeation extending upwards over the clavicle. If so, there should be a frequent association of enlarged supra-clavicular glands with the presence of subcutaneous nodules. These, however, were only found in seventeen per cent. of cases with enlarged supra-clavicular glands, as compared with eighteen per cent. of all cases. It seems certain, therefore, that in accordance with received opinion the efferent lymphatics which pass from the axillary to the supra-clavicular glands are the channels of infection of the latter set of glands.

Permeation of Lymphatic Plexuses.

We have seen that neither the direct nor the reflux lymph stream is capable of transporting cancer particles to points lying outside the lymphatic area in which the primary growth originated. The direct lymph stream is filtered of its cancer cells at the first set of glands, the reflux stream is similarly filtered in the fine anastomotic plexuses through which it must pass to adjoining lymphatic areas. Thus the lymph stream is ineffective as a means of *general* dissemination, it is effective only within the limits of the lymphatic area where the primary focus is situated. In whatever direction the cancer cells attempt to leave that area, they find an efficient filter blocking the way. How do the cancer cells overcome the resistance thus interposed and reach other lymphatic areas? The solution of the problem would evidently supply the key to dissemination.

In connection with this question I would like for a moment to call attention to the behaviour of porcelain filters with respect to certain micro-organisms. Mr. Kenneth Goadby informs me that bacteria, which cannot by any degree of pressure be forced through a porcelain filter, will nevertheless in a few days, if left within the filter, grow through its pores and infect its outer surface. It is similarly by the aid of their own proliferative power that cancer cells succeed in traversing the pores of the lymphatic filter in which they are imprisoned. It is a recognised fact that cancer cells traverse lymphatic glands in this way. But this centripetal route of invasion is relatively unimportant because it finally conducts the cancer cells to the blood, where they usually disappear harmlessly.

In a precisely similar way, but in a reversed direction, by actual centrifugal growth along the small lymphatic vessels in the neighbourhood of the primary neoplasm, cancer cells ultimately succeed in penetrating the fine anastomotic plexuses which, at the periphery of the lymphatic area concerned, bar the way into surrounding lymphatic areas. The evidence for this statement will be found in Chapter IV.

To the process of actual cancerous growth along the fine lymphatic vessels I have ventured to attach the name *lymphatic permeation*, or simply *permeation*. It appears to me to be the master process of dissemination. For whereas in attempted embolic dissemination *via* the glands the migrating cells are cast away in the blood, cancer cells which migrate by way of the peripheral anastomotic plexuses simply pass into the lymphatic vessels of adjoining areas without changing their conditions of life. Advancing in this way, slowly and centrifugally from one lymphatic area to the next, permeation may conceivably bring about the impregnation of the entire lymphatic system with cancer. An approximation to this condition is seen in the cases where subcutaneous nodules or bone deposits spare only the distal portions of the limbs.

The spread of cancer cells in the lymphatic plexuses to a large extent obeys the same laws as determine the mode of spread of a fluid such as mercury used for lymphatic injection.

Under the influence of pressure both the mercury and the cancer cells follow the lines of least resistance. But since in the case of the cancer cells the driving force is an internal pressure resulting from their own proliferation, it is not quite correct to speak of cancerous injection of the lymphatics; the process of permeation is rather one of tendril-like cancerous growth along the vessels. It is independent of the current of lymph, and proceeds with almost equal facility, either in the direction of, or against, the lymph stream, a fact which affords the key to the clinical puzzle that cancer is often seen to spread in a direction contrary to that of the lymph stream.

It is to be noted that permeation travels chiefly along the lymphatic vessels of medium size, avoiding at first the smallest lymphatic vessels, and only invading the large lymphatic trunks when the strong lymph current which scours their channel has been arrested by the growth of cancer in the glands to which they lead.

The anastomotic plexuses which divide the lymphatic system of the body into separate areas, and form effective barriers against retrograde embolic dissemination, are powerless to check the advance of permeation. In fact, so far as this process is concerned, the whole lymphatic system is a single network of accessible channels, and the slow centrifugal extension of permeation is often checked only by the death of the patient.

I have now to describe the details of this process, and to show why it has so largely escaped observation.

CHAPTER IV.

A MICROSCOPIC STUDY OF THE CENTRIFUGAL SPREAD OF PERMEATION IN THE PARIETAL TISSUES.

THE present chapter is an essay in the investigation of morbid processes, and in the co-ordination of minute and naked-eye morbid anatomy, by the application of microscopic methods on a macroscopic scale—a line of research which in my belief is capable of yielding valuable results, and even of giving a new impulse to the study of morbid histology.

For the convenience of the reader the conclusions concerning parietal dissemination reached in Chapter II. may here be recapitulated :—

(1) The study of secondary growths in the skin and subcutaneous fat, and in the bones, affords clear evidence of a slowly progressive, centrifugal, quasi-serpiginous spread of breast cancer in the parietes, in continuity with the primary growth, and independent of transport by the lymph or blood stream. This conclusion was based on the facts that (*a*) secondary growths are usually first observed in the immediate neighbourhood of the primary growth ; (*b*) though growth gradually spreads centrifugally from the primary focus the distal halves of the limbs enjoy a practical immunity from secondary deposits.

(2) The scattered and isolated character of the deposits in the skin and bones indicates that it is not along these layers that the growth primarily spreads.

(3) A study of the results of operation where (*a*) much skin and fascia, (*b*) less skin and more fascia, are removed strongly suggests that parietal extension does not take place primarily along the skin, but along the deep fascia, with secondary lateral offshoots towards the surface as subcutaneous

nodules on the one hand, and towards the deeper tissues as bone and muscle deposits on the other.

It is evident that these conclusions are only provisional, since they are derived merely from macroscopic and statistical evidence. It seems that the facts would be best explained by the continuous centrifugal growth of cancer along the meshes of the deep fascial lymphatic plexus into which many, if not all, of the breast lymphatics drain, and from which the trunks arise that convey lymph from the parietes to the axillary or to the inguinal glands. But though when present in its highest degree this process, to which I have ventured to apply the term "permeation," seems traceable by the characteristic distribution of the resulting naked eye metastases in the skin and bones, more frequently macroscopic evidence is dubious or wanting.

It was necessary, therefore, to test the hypothesis of centrifugal permeation by the microscope. This has been done by the examination of strips of the parietal tissues, radiating from the edge of the primary growth. In two cases, in order to minimise mutilation of the body, the strip examined was a median ventral strip in the line of the usual post-mortem incision. Though not accurately radial to the growth such a strip is sufficiently so for practical purposes. The layers included in the strips were skin, subcutaneous fat, deep fascia, and a superficial layer of muscle. From each strip, after fixation for a few days in 1 per cent. formalin to prevent separation of the overlying tissues from the deep fascia and muscles, a thinner strip, about $\frac{1}{8}$ inch thick was cut, in a plane vertical to the skin. In order to make this section as accurately as possible the strip was frozen hard before cutting.

The thin strip thus obtained was divided by transverse cuts into a number of blocks of suitable size. The end nearest the growth was marked in each block by a small cut in the skin surface. The pieces were then transferred, in order, to numbered bottles, hardened in alcohol, and embedded in paraffin. The resulting series of sections was stained with hæmatoxylin and eosin, and a microscopic view of the whole length of the original strip was thus obtained.

In one case (case ii.) a continuous series of from thirty to fifty sections was mounted from nearly every block of the two strips examined. In this case, therefore, over 500 microscopical sections had to be prepared and examined.

Five non-consecutive cases, now to be described, were more or less completely dealt with in this manner.

CASE I.

On the thorax in the region of the right breast is an ulcerated tumour as large as an orange. It is surrounded by isolated hard nodules, which occupy the axilla (under the pectoralis major), and fill up the right axilla itself, where they form a mass pressing on the axillary vein, and causing œdema of the arm.

Similar nodules are found in the left breast. The skin over the sternum between the breasts also shows a few small subcutaneous nodules. One large nodule is situated under the left pectoral muscle, but there are no enlarged glands in the left axilla. The supra-clavicular glands are palpable on the right side. There are no nodules on the skin of the back, abdomen, etc.

Three ribs beneath the right breast are completely infiltrated, and the right pleura shows numerous white hard nodules, especially on its parietal portion.

There are numerous nodules on the posterior aspect of the sternum. The right lung shows a few hard nodules; the left lung also, but to a less extent.

The liver presents several secondary nodules on its surface near the round ligament.

The parietal strip examined was a median ventral one, extending from 25 mm. below the suprasternal notch to a point 60 mm. above the umbilicus.

A slice 3 mm. thick, hardened and stained in Orth's fluid and cleared in xylol*, demonstrated very clearly that the growth was extending downwards, macroscopically at any rate, not along the skin but along the plane of the deep fascia. (See Frontispiece.)

* For a description of this method, which in my hands has given better results than Stiles' nitric acid method, see Archives of the Middlesex Hospital, Vol. iii., p. 35, and p. 29 of this book.

DETAILED MICROSCOPICAL EXAMINATION OF CASE I.

Taking the level of the umbilicus as a fixed point, and travelling upwards along the strip, we will now describe the conditions found at each level.

The distances are expressed in millimetres above the umbilicus. The foci between levels 160 and 188 mm. are shown in Fig. 13 under a low magnification.

(1) *Level* 0–60 *mm.*—Tissues not examined.

(2) *Level* 60 *to* 160 *mm.*—Tissues found entirely free from Cancer.

Zone of Fascial Permeation, Inflammatory Reaction Absent.

(See page 88.)

(3) *Level* 160 *mm.*—Two minute lymphatics each about 60μ in diameter, containing groups of cancer cells, lying upon the anterior layer of the Rectus sheath (see Fig. 15). There are no leucocytes either within or around the invaded lymphatics. A normal minute blood vessel lies near them.

(4) *Level* 161·2 *mm.*—A gaping space lined by endothelium and situated upon the deep fascia. By comparison with other sections it is clear that this is a lymphatic from which a group of cancer cells has fallen out.

(5) *Level* 166 *mm.*—Two lymphatics filled by cancer cells in the deepest layer of the subcutaneous tissue, lying near a normal artery. Close to these are two minute nodules of cancer, the largest ·8 mm. in diameter.

(6) *Level* 167 *mm.*—Two lymphatics, respectively 160 and 80μ in diameter, lying on the deep fascia, and filled by cancer cells. There are no leucocytes in the neighbourhood. The cancer cells in the larger vessel, except those lying next the endothelium, are swollen, degenerate and highly refractile, and stain imperfectly. The lines of separation between adjacent cancer cells are very sharply defined.

(7) *Level* 172·6 *mm.*—Lying on the rectus sheath close to normal blood vessels in which red corpuscles can be seen, is a group of three minute lymphatics, the largest about 70μ in diameter, each containing groups of cancer cells. Close to these on the surface of the fascia is a minute cancer nodule

about ·25 mm. in diameter. The appearances suggest that this originated from the rupture of a lymphatic by the growing mass of cancer cells within it. Only very few leucocytes are present near the invaded tissues.

(8) *Level* 175·6 *mm.*—An oval space 250μ in mean diameter, lying on the rectus sheath, and apparently lined by endothelium. It is filled by cancer cells which towards the centre are swollen, hyaline, degenerate, and polygonal from mutual pressure, though their nuclei still stain fairly well. The peripheral layer of cancer cells is not degenerate. The space appears to be a lymphatic distended by cancer cells, but not to the point of rupture. On one side of the permeated lymphatic is a small aggregation of leucocytes.

(9) *Level* 176·9 *mm.*—On the surface of the rectus sheath is a cancerous lymphatic, 140μ in diameter, with a thin wall consisting only of endothelium with well-stained nuclei. Some of the cells in the centre of the group are beginning to degenerate. Near the lymphatic is a group of normal minute blood vessels, round which are a few emigrated leucocytes. There are no leucocytes in the immediate neighbourhood of the permeated lymphatic.

(10) *Level* 178·6 *mm.*—On the rectus sheath is a lymphatic 90μ in diameter, lined by definite endothelium, and filled by cancer cells, which have somewhat shrunk away from its walls. Leading from it right through the rectus sheath to its muscular aspect is a minute vessel lined by endothelium, evidently a branch lymphatic, into which growth has not penetrated. There are no leucocytes near the permeated lymphatic (Fig. 16).

(11) *Level* 178·6 *mm.*—A small lymphatic full of cancer cells lying on the anterior layer of the rectus sheath.

(12) *Level* 182·6 *mm.*—Oval section of an endothelium-lined lymphatic, 110μ in diameter, lying upon the anterior layer of the rectus sheath, and filled by cancer cells that stain well and show no signs of degeneration. Near it is a group of minute blood vessels, around which are about a dozen emigrated leucocytes.

(13) *Level* 182·9 *mm.*—An endothelium-lined lymphatic, 150μ in diameter, lying on the rectus sheath, and distended by cancer cells. The central cells are degenerate. At one side

the lymphatic vessel has apparently ruptured, and the cancer cells are beginning to infiltrate the adjacent tissue. There is no leucocytosis.

Zone of Fascial Permeation, Perilymphatic Leucocytosis present.

(14) *Level* 184·5 *mm.*—On the anterior surface of the rectus sheath is an oval empty space 45μ in diameter, lined only by rough fibrous tissue, though on one side there appear to be traces of endothelium. It possesses no proper wall of its own, and contains only a few scattered red corpuscles, and a group of cancer cells adherent to its wall at one point. On the deep aspect of this space the rectus sheath is infiltrated by groups of cancer cells nearly to its muscular surface. The blood vessels in the neighbourhood are crowded with leucocytes, and there is a commencing leucocytic invasion of the carcinomatous cell groups.

The appearances here may, but probably do not, represent the invasion of a vein by cancer. The large space has no definite coats, and is almost certainly a lymphatic which has ruptured owing to hyper-distension by cancer cells (cf. Fig. 20). This rupture is associated with slight traumatic hæmorrhage, and with inflammatory reaction which encapsules the cancer cells. Definite inflammatory reaction here shows itself for the first time.

(15) *Level* 185·3 *mm.*—Diffuse infiltration of the rectus sheath nearly to its deep surface by cancer cells lying singly or in groups. They stain badly, are surrounded by a crowd of leucocytes, and are apparently being destroyed.

(16) *Level* 186 *mm.*—A space 500μ in diameter, lying on the anterior layer of the rectus sheath, exactly similar to that described at level 184·5 mm. It contains, however, in addition to some few red blood corpuscles, a larger group of degenerate cancer cells. The leucocytic reaction in the surrounding tissues (which as in the former case are infiltrated by groups of cancer cells) is rather more marked. It is noticeable, too, that many of the cancer cells, even in the smaller groups, have completely degenerated into a hyaline unstained material.

(17) *Level* 187 *mm.*—Two endothelium-lined lymphatics each about 125μ in diameter, on the superficial aspect of the rectus sheath, permeated by somewhat degenerate cancer cells. A slight hæmorrhage has taken place into one of them, though at the level of the section no rupture can be seen. A few isolated cancer cells are present in the neighbouring tissues, together with some emigrated leucocytes.

(18) *Level* 188·3 *mm.*—A large oval space, 1·5 mm. in its long diameter, possessing a definite but very thin wall, which, though in places showing traces of an endothelial lining, seems to consist chiefly of young nucleated fibrous tissue mixed with cancer cells. This space may possibly be an invaded vein, but almost certainly it represents an invaded and ruptured lymphatic, with a wall of newly formed fibrous stroma. For in a nodule of cancer situated in the muscle higher up there is an exactly similar space lying quite close to an artery and vein, neither of which is invaded by growth.

The space contains a mass of cancer cells, now somewhat shrunken, which, no doubt, during life completely filled it, There are, however, here and there around the mass of cancer cells some altered red blood corpuscles. The peripheral cells of the cancerous mass are vigorous and stain well, while the central cells are swollen and hyaline, and in places entirely converted into an unstained granular material. There is a slight leucocytic reaction in the tissues round the space.

(It should be noted that up to this point cancer occurs only in, upon, or just over, the deep fascia, and has not invaded either skin or muscle.)

Zone of Perilymphatic Fibrosis, with early Nodular Deposits.

(19) *Level* 188·5 *mm.*—In the subcutaneous tissue is an oval annular area of fibrous tissue, about 125μ in diameter, enclosing cellular débris. In the centre of this débris are a few cells which show all the characters of carcinomatous epithelium.

(20) *Level* 189·5 *mm.*—Lying just beneath, but not actually reaching the surface of the transversely cut muscle (pectoralis) seen at this level, there is a nodule 2 mm. in diameter. It is

bluntly conical in shape, with its apex directed towards the deep fascia, and is connected therewith by a fibrous septum, in which some microscopic sections show a lymphatic containing a mass of degenerate cancer cells.

(21) *Level* 190·1 *mm.*—In the subcutaneous tissues over the deep fascia at this level there is a small normal artery and vein. Touching them is a small circular area of concentrally arranged fibrous tissue, enclosing some cellular débris.

(22) *Level* 190·1 *mm. to* 196·3 *mm.*—In this part of its length the subcutaneous tissue down to the deep fascia shows at short intervals, especially along its fibrous septa, circular, oval, and strap-shaped areas of fibrous tissue. Many of these areas enclose either stained cells, sometimes recognisable as cancer cells, or they contain cellular débris. Some of the areas consist entirely of fibrous tissue. The muscle is normal, except for one or two lymphatics filled with cancer cells.

(23) *Level* 196·3 *mm.*—At this level the skin shows cancer for the first time. There are two spaces in the dermis lined by endothelium, which contain degenerate cancerous epithelium. Near them are a few cancer cells lying interstitially. From this point for 6 mm. upwards the deeper layer of the dermis is more or less invaded by growth which is partly intra-lymphatic, partly interstitial. The appearances in the subcutaneous tissue are unchanged. Some of the fibrous areas in it have a glandlike appearance, and may possibly be outlying lobules of breast tissue, but this is certainly not the case with most of them.

(24) *Level* 199 *mm.*—A large cancer-filled lymphatic in the deep subcutaneous tissue close to the fascia.

Zone of Nodules, Permeated Lymphatics destroyed.

(25) *Level* 199 *mm. to* 224 *mm.*—In this region the cancer process is so far advanced that it becomes needless to trace it microscopically. As one passes upwards, the cancerous masses, becoming larger, at length involve all the layers indiscriminately. Permeated lymphatics can still be seen here and there among the nodular and often apparently isolated deposits.

It is noticeable that macroscopic nodules in the muscle occur much further down, i.e. further away from the growth, than do macroscopic nodules invading the skin.

(26) *Level 224 mm.*—We have now arrived at the approximate level of the nipple and of the primary growth. Near this point is a skin nodule about 1 mm. in diameter, the only one visible to the naked eye in the strip examined. Since the strip, though reaching higher than the primary growth, did not at its upper limit extend as far as the microscopic growing edge of the carcinoma, it is useless to trace it further.

Summary of Microscopic Examination of Case I.

The microscopic growing edge of the cancer reaches to a point about 1½ inches below the ensiform cartilage. Below this point the tissues are quite free from growth, while above it they show foci of cancer at short and fairly regular intervals. The lower limit of the pectoral fascia has not in any way barred the downward course of the growth. At one point the cancer has penetrated the anterior layer of the rectus sheath nearly to its deep surface, Had the section passed through the linea alba, cancer cells would doubtless at this level have been seen in ominous proximity to the subperitoneal fat and peritoneum.*

For a breadth of over 30 mm. the microscopic margin of the carcinoma lies exclusively in the plane where the deep fascia joins the overlying fat (see Fig. 13).

The microscopic growing edge, traced from the periphery towards the primary growth, presents the following zones, each of which merges gradually into the zone on either side of it:—

(1) *Zone of Permeation of the Deep Fascial Lymphatic Plexus.*—This zone presents two subdivisions. In its peripheral portion inflammatory reaction is absent. The lymphatics forming the plexus are seen at short intervals as spaces lined by endothelium and containing cancer cells in an active condition. The lymphatics are not distended, and

* The subject of "Epigastric Invasion of the Abdomen" is dealt with at length in Chapter V.

there are no leucocytes around them. In the proximal portion of the zone of permeation the lymphatics show increasing distension by the growing cancer cells, which themselves are undergoing degeneration from the increased pressure produced by their proliferation. Around the invaded lymphatics are seen collections of inflammatory round cells Still nearer to the inner margin of the zone are seen large spaces containing cancer cells and a few red blood corpuscles. It will be shown later that these spaces are formed by the rupture of the distended lymphatics.

(2) *Zone of Fibrosis around the Permeated Lymphatics (Perilymphatic Fibrosis), with Destruction of the Cancer Cells contained in them.*—In consequence of this process the adjoining layers—first the muscle, and later the skin—show commencing nodular invasion, which is brought about in a way to be presently described.

(3) *Zone of Discrete Nodular Deposits in all the Parietal Layers.*—As the primary growth is approached these deposits become more massive and numerous. The sporadic distribution which they often seem to show results from fibrous obliteration of the permeated lymphatics which formed the lines of communication with the primary growth. In this zone the cancer process is so far advanced that its earlier stages can only be traced inferentially from the appearances nearer the growing edge.

Beyond this zone is the primary growth proper, which may be defined as the region of interstitial infiltration round the original focus.

CASE II.

In the site of the right breast was a fungating crateriform mass as large as a man's hand, extending from the second down to the sixth rib, and obliquely from the parasternal line to the anterior fold of the right axilla. In continuity with the tumour some glands were found in the right axilla, and there was marked œdema of the right arm.

Independently of the first tumour, the left mamma was enlarged (probably secondarily) and showed a conical tumour adherent to the skin. Several cutaneous nodules of the size

of a pea were scattered round the principal mass on the left side of the thorax, but there was no ulceration present. The left axillary glands were involved, but there was no œdema of the left arm. There was an enlarged gland of the size of a walnut above the right clavicle. The right pleura showed some white prominences at the level of the right breast, where two ribs and the intervening muscles were completely invaded by the growth. Posteriorly there were some small scattered growths on the parietal pleura, especially in its lower part.

The lumbar glands were not enlarged, but were white on section, as if containing new growth. One portal gland the size of a hazel nut appeared distinctly malignant. Some malignant deposit occupied the anterior border of the right lobe of the liver, and several nodules were scattered through its substance.

Two parietal strips were taken from this case, one running outwards along the arm, the other downwards and backwards into the loin; so as to institute a comparison of two radial sections of the growing edge chosen at random.

The proximal portion of these strips presented to the naked eye an almost continuous series of subcutaneous nodules lying along the line of junction of the dermis with the subcutaneous fat, and infiltrating the overlying dermis. The deeper tissues appeared to be quite free from growth. It seemed evident, *primâ facie*, that the growth was spreading along the plane of the deep cutaneous plexus. This fact lent special interest to the case, since I had previously met with no evidence to support the belief that breast cancer spreads along this hypothetical plexus, whose existence is strongly denied by Sappey.

Strip A.—Extending for 90 mm. from the Outer Edge of the Ulcerated Mass of Growth and Downwards along the Right Arm.

The strip was divided into six blocks, four of which were cut in series. About 250 sections were in all examined.

Skin.—The condition of the skin need not be described in detail. It is invaded more or less continuously along its

whole length by confluent nodules which diminish in size and become microscopic, until at 84 mm. distance from the edge of the malignant ulcer, and 1 mm. beyond the microscopic edge of the cancer in the deep fascia, the last minute nodule is seen. Beyond this point the skin is free from growth.

Along the proximal five-sixths of the strip the skin which intervenes between neighbouring skin nodules shows lymphatic and interstitial invasion by cancer cells. The distal 8 mm. of the invaded portion of skin is free from cancer, except for two isolated skin nodules at the deep aspect of the dermis.

Subcutaneous Tissues.—There are in the subcutaneous tissues a few nodules visible to the naked eye. Permeated lymphatics are to be seen here and there, generally close to the nodules.

Deep Fascia.—All the foci of cancerous growth found in the deep fascia are included in the following description. The figures represent distances from the ulcerated edge of the growth.

Zone of Nodules, Permeated Fascial Lymphatics partially or completely Fibrosed.

0 *to* 10 *mm.*—Fascia missing from the strip.

27·5 *mm.*—Lying upon the fascia are a small artery and vein, the former surrounded excentrically by a dense area of fibrous tissue.

38 *mm.*—A fibrous area surrounding a small artery and vein is seen at this point.

45·5 *mm.*—An oval area, 1 × ·25 mm. in diameter, of concentrically arranged nucleated fibrous tissue, enclosing a few undoubted degenerate cancerous cells. This is the focus of fascial cancer nearest to the primary growth.

45·5 *to* 63·5 *mm.*—No recognisable foci of cancer.

From 63·5 *mm.*—Fascial foci are seen at the following points:—

63·5 *mm.*—A lymphatic about 100μ in diameter, lying near a small artery. It is filled by vigorous cancer cells, which at one point have ruptured its wall, and are commencing to invade the surrounding tissue. There are but few leucocytes in the neighbourhood. In another section of this series the

lymphatic is replaced by two smaller ones, and has evidently bifurcated.

72·5 *mm.*—Close to a small vein is a group of about 20 cancer cells. Some of them are degenerate and are apparently being destroyed by the fibrous tissue which surrounds them.

Zone of Fascial Permeation.

76 *mm.*—A lymphatic full of vigorous cancer cells in the deep subcutaneous tissue. It is 160μ in diameter, and is lined by endothelium. No leucocytic reaction.

77 *mm.*—A cylindrical mass of vigorous cancer cells, 100μ in its short diameter, and 800μ long, lying in a space lined by endothelium. No sign of inflammatory reaction round the space. It is evidently a lymphatic in longitudinal section, since normal blood-vessels can be seen quite close to it.

78 *mm.*, 79 *mm.*, 81 *mm.*, 83 *mm.*—At each of these points a narrow permeated lymphatic, filled but not distended by cancer cells, is seen either in transverse or longitudinal section. The carcinomatous epithelium exhibits no signs of degeneration. (Fig. 14 represents this region.)

83 *to* 90 *mm.*—Fascia free from cancerous invasion.

Muscle.—Along this strip the muscle appears to have entirely escaped invasion.

SUMMARY OF HISTOLOGICAL EXAMINATION,

Strip A.

From the edge of the ulcerated growth down the right arm cancer had extended microscopically in the deep fascia for 83 mm., and in the skin for 84 mm. Beyond this point the tissues showed no cancer, and especially no isolated foci such as might result from embolism.

The invaded length of deep fascia is clearly divisible into two zones:—

(a) The peripheral zone, which forms a narrow microscopic growing edge about 7 mm. wide, in which the fascial lymphatics are full of vigorous cancer cells, and are not yet ruptured, nor even much distended, by the growth within them. (Fig. 14 represents this zone.)

(b) The proximal zone, about 76 mm. wide, in which a process of perilymphatic fibrosis is going on, which ends in the destruction of the permeated fascial lymphatics, and their replacement by solid threads of fibrous tissue. This process can be seen half completed in the focus at level 45·5 mm., where the appearances are similar to those shown in Fig. 21. For the most part, however, fibrosis has proceeded so far that the deep fascia shows cancer foci only at very few points. The fibrous areas free from cancer round several of the blood vessels towards the proximal end of the strip undoubtedly represent the termination of the process of perilymphatic fibrosis.

Opposite to the microscopic growing edge of the cancer—i.e. in the zone of permeation—the skin showed merely two very minute nodules. These nodules were isolated from each other. A permeated lymphatic was traced obliquely in a distal direction from the deep fascia of the *proximal* zone towards one of these nodules (see Fig. 14). They were not apparently connected with the distal zone of permeation, but simply overlapped it. It is therefore probable that the invasion of the skin was consequent on invasion of the deep fascia, not *vice versâ*. This question will be discussed later.

Strip B.—Extending for 83 mm. from the Lower and Outer Edge of the Ulcerated Mass of Growth Downwards and Backwards across the Lower Ribs and Lumbar Fascia.

The strip was divided into seven blocks, the majority of which were cut in serial section, so that not only was the strip examined in its whole length, but for an appreciable portion of its width. In all about 200 sections from it were examined.

In the description which follows the figures refer to the distances from the ulcerated edge of the growth.

Skin.—The naked-eye and microscopic appearances of the skin were identical with those seen in Strip A. The skin is invaded for 49 mm., i.e. for exactly the same distance as the deep fascia. Between the closely set subcutaneous nodules,

whose size varied inversely as their nearness to the primary growth, the skin showed interstitial or lymphatic growth to a greater or less extent. From 36 mm. to 49 mm., however, there is no continuity in the cutaneous foci. In this stretch of tissue only two minute skin nodules are visible, with permeated lymphatics near them. Moreover these nodules are not present in all the sections.

The invasion of the skin in the distal portion of the strip has therefore a discontinuous character, while, on the other hand, invasion of the fascial plexus in the distal portion of the strip is emphatically by continuous growth. In Case II. therefore, though less decisively than in Case I., the evidence points to the spread of cancer, not along the skin, but along the deep fascia with secondary vertical efflorescences towards the other layers.

Subcutaneous Tissues.—A few nodules are present here and there in the subcutaneous fat. An occasional permeated lymphatic can be seen. Sometimes the "tail" of a skin nodule is continued down into the deep tissues by such a permeated lymphatic.

Deep Fascia.—The deep fascia is invaded by the centrifugal growth of cancer along its lymphatic plexus. The invaded area is divisible into two zones, a peripheral one of lymphatic permeation and a proximal one where the permeated lymphatics are partially or completely destroyed by perilymphatic fibrosis.

In this strip two strong fascial layers, separated by a thin layer of fat, were present over the muscles. Most of the permeated lymphatics lay in the more superficial of these layers.

Zone of Nodules, Permeated Lymphatics partially or completely Fibrosed.

0–7 *mm.*—Deep fascia missing from the strip.

9 *mm.*—A circular mass of nucleated fibrous tissue, enclosing in its meshes a few degenerate cancer cells, and surrounding what appears to be a ruptured lymphatic containing similar cancer cells. This fibrous area lies at the point of junction of a fibrous septum with the deep fascia. Above,

the fibrous septum runs into the "tail" of a subcutaneous cancer nodule (Figs. 25 & 26).

10 *mm.*—A similar fibrous area, about 600μ in diameter, enclosing a large number of degenerate cancer cells (Fig 22). At the other end of the series of sections taken from this particular block, this area is almost entirely fibrous, and contains only one or two cancer cells (Fig. 23). Its diameter has decreased to 300μ.

14–19 *mm.*—Deep fascia missing from the section.

25 *mm.*—In the deep subcutaneous tissue, lying close to a large artery, are two minute lymphatics containing a few degenerate cancer cells. Just superficial to these is another permeated lymphatic, in which the central cells are swollen and degenerate, while the layer of cells touching the endothelium stains well. There is interstitial invasion of a well-defined area of fibrous tissue which surrounds the lymphatic, but at this level no rupture can be seen in the wall of the vessel. Still nearer the skin is a subcutaneous nodule 1 mm. in diameter not reaching up to the dermis.

28 *mm.*—A lymphatic about 160μ in diameter containing degenerate cancer cells. Close to it is a group of cancer cells lying interstitially, which have apparently escaped through a rupture in the wall. There are a few leucocytes near the cancer focus.

29 *mm.*—A space 500μ in diameter, lined by endothelium. It is filled by degenerate cancer cells, and is probably a distended but still unruptured lymphatic.

31 *mm.*—A similar lymphatic in oval section, 500 by 100μ.

35 *mm.*—A distended permeated lymphatic, 600 by 150μ. At one point the wall has given way and the cancer cells are beginning to pass into the tissues. At this point the mass of cancer cells is being invaded by leucocytes.

Zone of Permeation.

35·5 *mm.*—A small cancerous lymphatic 150μ in diameter.

38 *mm.*—A space 600 by 200μ, filled by degenerate cancer cells and lined, at any rate partially, by endothelium. At this

level a permeated lymphatic can be traced in longitudinal section for some distance into the muscle.

39 *mm.*—A group of cancer cells, measuring about 500μ in diameter, showing marked leucocytic invasion and fibrosis. Some of the cancer cells still look vigorous.

43·5 *mm.*—Throughout a series of sections there is a focus of cancer at this level. Its character, however, varies considerably. In some sections one or more cylinders of cancer cells are seen, measuring about 35μ in their short diameter. These are evidently lymphatics filled but not distended by cancer cells. In other sections an oval area of cancer cells about 200μ in diameter is visible, with a narrow permeated lymphatic running out of it.

49 *mm.*—In some of the sections, but not in all, narrow lymphatics, filled but not distended by cancer cells, are seen at this level. In other sections again, an oval area of cancer cells 150μ in its short diameter is present at the same level. Possibly these expansions represent the nodal points of the fascial plexus.

49 *mm. to* 83 *mm.*—Tissues free from cancer along their whole length. In order to examine the breadth as well as the length of the strip, a series of sections taken from the block just beyond the microscopically determined growing edge was carefully examined. No cancer was found in any section of the series, while it was present in every one of the sections taken from the preceding block.

Muscle.—The muscle seems to have escaped invasion entirely, except at one point. About 38 mm. from the proximal end of the strip, in some of the sections, a small permeated lymphatic can be traced for a long distance down into the substance of the muscle. The point where this lymphatic was found must have been in the lumbar region, just below the 12th rib. Since the parietes are very thin, cancer might thus invade the perinephric fat and reach the lumbar glands.

Among 329 autopsies on breast cancer at the Middlesex Hospital during the last thirty years, I found six in which the kidneys, suprarenal capsules, or lumbar glands were invaded without other abdominal metastases, and without thoracic metastases. In three of these cases subcutaneous nodules, an

index of wide parietal dissemination, were present. Subcutaneous nodules were found in only 22 per cent. of the whole number of cases. These statistical facts lend an interest to the preceding observations (see p. 135).

COMPARISON OF STRIPS "A" AND "B."

The absolute distance of the microscopic edge of the growth from the margin of the ulcer was in the case of Strip A, 84 mm.; in the case of Strip B, 49 mm. On the centrifugal hypothesis these distances should be approximately equal if measured from the actual point of origin of the growth, but this precise point could not be determined. The area of centrifugal spread is of course not a mathematical circle.

Microscopically the appearances indicated that permeation was extending rather more rapidly down the arm than into the loin. But the appearances in the two strips were in all important respects identical. The qualitative identity of two radial sections extending from the growth in widely divergent directions, chosen at random, amounted to an almost complete proof of the centrifugal hypothesis for this particular case.

COMPARISON OF CASE II. WITH CASE I.

This case differs from the preceding one in several important respects, while it nevertheless shows the same processes at work. In Case II. the proliferation of the cancer cells was evidently less rapid, and the inflammatory reaction was more successful in checking and limiting dissemination.

The zones traceable round the primary growth are the same as in the previous case, but they are not so well defined. The zone of permeation, though well marked in both strips, is a very narrow one, and consequently the cutaneous efflorescences belonging to the zone of fibrosis actually overlap it in some sections. On the other hand the zone of partial perilymphatic fibrosis is a very wide one, and is not clearly marked off from the zone of nodules with completely fibrosed lymphatics. The latter corresponds to the peripheral part of the large cancerous ulcer, and to the proximal portions of the strips examined. In the case of Strip A only a single obsolescent focus of cancer was present on the deep fascia in

the first 63 mm. of its length. Only two similar foci were present in the first 28 mm. of the length of Strip B.

The destruction of the permeated fascial lymphatics is better seen than in Case I., because it was not obscured by rapid and extensive formation of nodules in the adjoining layers.

But the main importance of the case lies in the fact that it demonstrates the various stages of perilymphatic fibrosis at different points along the length of the same lymphatic (Figs. 22 and 23).

CASE III.

A recurrent ulcerating scirrhus of the right breast, with metastases in the thorax and abdomen. A nearly vertical strip of tissue extending downwards from the ulcer was examined by means of horizontal sections taken at intervals along its length. Unfortunately it did not in its whole length include all the layers of the parietes. Subcutaneous nodules were present, the lowest of which was situated eight inches above the umbilicus. A section of the skin half an inch above this nodule, between it and the primary growth, was absolutely free from cancer; there was, therefore, no continuity of infection along the skin. The dermis around the nodule was only infiltrated for a very short distance.

Two and three-quarter inches below this nodule the small lymphatics lying upon or in the anterior layer of the rectus sheath were found blocked by lines of cancer cells, while the subcutaneous tissue up to the dermis was quite free from growth. Sections, three in number, taken at intervals above this point, showed more advanced infection of the deep fascia, as the primary growth was approached.

Seven sections taken at intervals below the lowest point where the deep fascia was found infected, showed that the tissues beyond this point were entirely free from growth, at any rate down to one inch below the umbilicus.

The histological examination in this case, imperfect though it was, showed that invasion of the deep fascia extends a long way beyond the remotest subcutaneous nodule. It proved that healthy skin may intervene between adjacent cutaneous

metastases, and suggested that the cancerous process in the deep fascia is one of actual continuous growth along lymphatic vessels. The absence of isolated foci of growth below a definite level above which no section of deep fascia free from growth was found, was much opposed to the embolic view of the spread of cancer in the deep fascia.

This case is inserted because it confirms in some particulars the conclusions arrived at from consideration of Cases I. and II.

CASE IV.

The right breast had been removed for cancer. There was no ulceration of the scar. Subcutaneous nodules were present in large numbers, and were arranged in definite lines radiating from the right axilla. They did not cross the middle line except on the abdomen, where a few small ones could be felt in the left hypochondriac region. One definite line ran directly upwards across the junction of the middle and outer thirds of the clavicle, and was continued in the posterior triangle of the neck. A second ran horizontally outwards across the deltoid muscle. Four lines of nodules, diverging somewhat as they descended, ran downwards from the axilla over the lateral aspect of the thorax. One of these lines descended direct to the inguinal glands; it was formed of half a dozen large nodules in the thoracic region, of a single large one about the level of the umbilicus, and of a tiny *fascial* nodule, not involving the skin, about three inches above Poupart's ligament. There were nodules also in both scapular regions and in the loins. A nodule of growth was found in the left breast, and in each of the lateral lobes of the thyroid. The axillary, supra-clavicular and inguinal glands on both sides were cancerous. The left clavicle was fractured. Visceral metastases were present in the chest.

The histological examination of the case was imperfect. Permeated lymphatics were found upon and in the deep fascia one inch above Poupart's ligament. Near this point a vertical cord of growth, evidently a permeated trunk lymphatic, was visible, running downwards to the inguinal glands. An inch higher up the tissues were invaded up to the dermis. Several

permeated lymphatics were also detected in sections taken three inches above the costal margin, just to the right of the middle line.

A section of a muscular nodule to the right of the middle line just below the costal margin, showed cancer cells lying between the fibrous bundles of the rectus sheath, but no permeated lymphatics were seen either in this situation or (*a*) an inch above the xiphoid cartilage just to the right of the middle line; (*b*) an inch below the xiphoid cartilage; (*c*) two inches below the umbilicus.

In this case the process of centrifugal spread seems to have recommenced from a focus of growth in the right axilla left behind at the time of the operation.

The scarred area left by the operation seems to have hindered the extension of nodules to the left side of the body, but, nevertheless, the case illustrates their centrifugal spread.

Fascial permeation is here seen extending beyond the remotest visible subcutaneous nodule, and at a great distance from the original focus of growth.

The case, though imperfectly examined, is inserted to show how widely permeation may extend. In Case I. the process of permeation, though it had extended downwards over the abdominal wall, had not crossed the water-parting which separates the lymphatic area of the axillary glands from that of the inguinal glands. This water-parting or neutral zone between the contiguous lymphatic areas corresponds to a horizontal line running through the umbilicus. It is a region of fine anastomoses, nowhere traversed by trunk lymphatics, admirably adapted to filter off any cancer cells which attempt to reach the inguinal glands by a reflux lymph stream. The present case shows that permeation is capable of penetrating through this neutral zone into adjoining lymphatic areas. This appears to be the essential event of dissemination.

The freedom of the deep fascia from permeation at points near the growth, and its presence at points further removed from it, are explained by Cases I. and II., which show that fibrosis follows permeation, and that the growing edge may advance as a ring, within whose inner margin the evidence of permeation has vanished.

CASE V.

The patient first began to ail nine or ten months before death. Six months before death a lump was felt in the left breast. Jaundice supervened six weeks before death. At this time large glands were present in both groins and in both axillæ, along with very numerous nodules in the subcutaneous tissue. The largest nodules were near the breast, and at the back of the neck, and many of these were adherent to the skin. Diminishing in size and losing their adhesion to the skin, they reached over the abdomen nearly down to the groins, but there were no nodules on the lower limbs. Very tiny fascial nodules could be felt in the left arm down to the elbow, along the line of the axillary vessels, and half way down the right upper arm. Fairly large nodules were present on the neck, a few on the scalp, and on the side of the face. (Fig. 11.)

The subcutaneous tissue of the left arm conveyed to the examining hand a markedly different sensation above and below the elbow. On the upper arm the tissues felt distinctly granular apart from the separately palpable nodules, while below the elbow the tissues were perfectly smooth, soft, and normal.

At the autopsy a still more extensive distribution of nodules was found. They were universally, though irregularly, distributed over the body, except on the distal portions of the limbs. The remotest nodules, minute shotty lumps on the deep fascia, were situated as follows:—

On the summit of the scalp, 18 in. from the primary growth.

On the left arm, 1 in. above the elbow, 11 in. from the primary growth.

* On the right arm, 1 in. below the elbow, 19 in. from the primary growth.

* On the left thigh, 6 in below the anterior superior spine, 18 in. from the primary growth.

* On the right thigh, 7 in. below the anterior superior spine, 21 in. from the primary growth.

The lowest nodule on the back was situated over the 2nd sacral spine, 15½ in. from the primary growth.

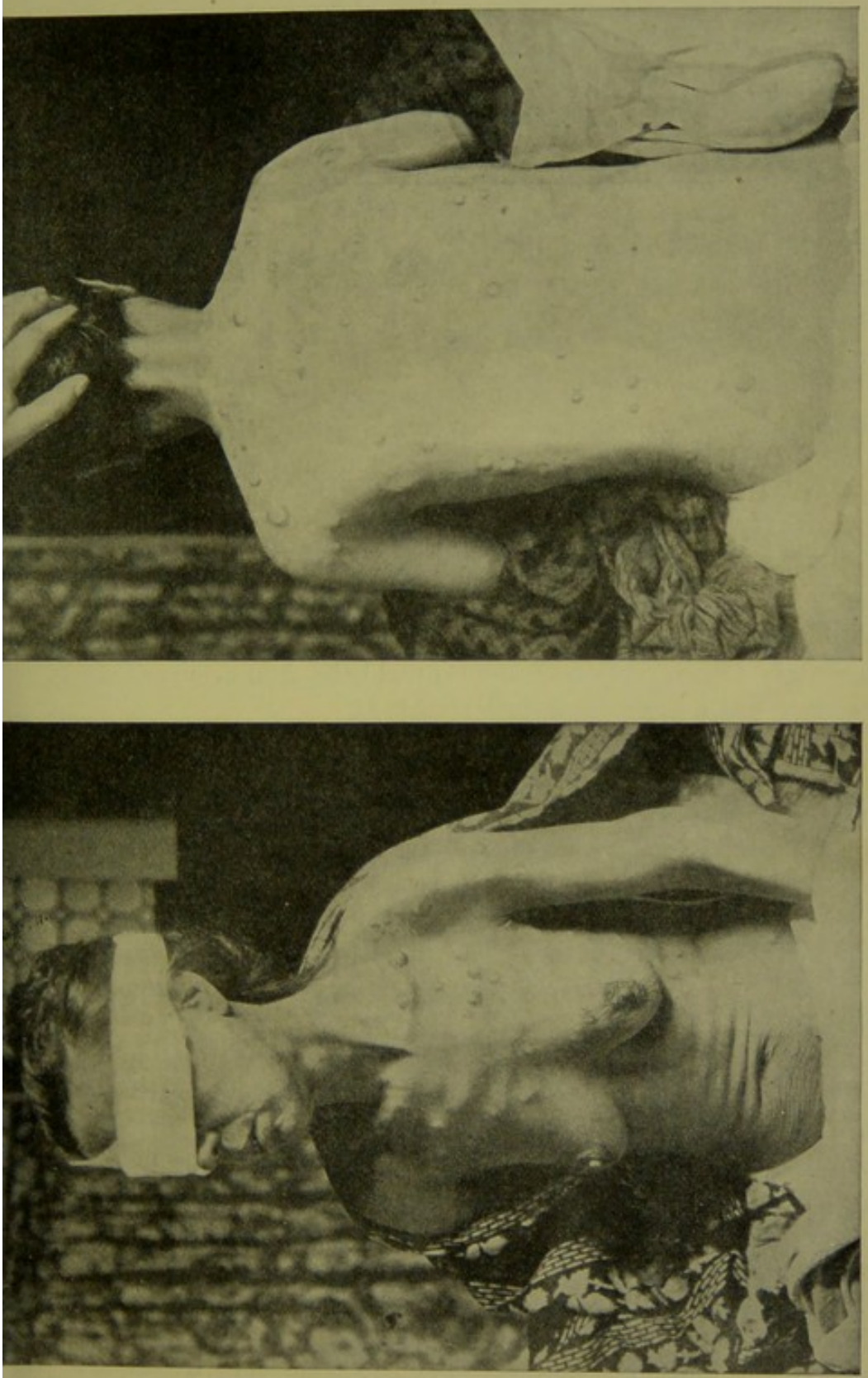


Fig. 11 illustrates the centrifugal spread of subcutaneous nodules, and is taken from a case of cancer of the left breast at the Samaritan Hospital under the care of Mr. Corrie Keep. (Case V.)

There was a nodule above the right posterior superior spine, 17 in. from the primary growth.

There was a nodule above the right iliac breast, 15½ in. from the primary growth (measured round the right side of the body).

In the situations marked with an asterisk (*) nodules certainly became recognisable only during the last fortnight of life. The largest nodules were situated at the back of the neck, in the scapular regions, over the front of the chest, and over the left clavicle. Upon the abdomen they were small and thinly scattered.

There were in this case numerous visceral metastases, the distribution of which does not concern us. Microscopically the growth was diagnosed as an endothelioma, a type of neoplasm particularly likely to show lymphatic spread, in consequence of its genetic relations with lymphatic channels. Its cells were of moderate and uniform size, with round vesicular nuclei. When aggregated together in alveoli, many of the central cells showed marked vacuolation. In places complete disintegration of the central cells had occurred, and nothing but a granular débris remained.

On the clinical and macroscopic side the case showed conclusive evidence of rapid centrifugal dissemination. A fortnight before death, for instance, no nodules were found on the thighs, while at the autopsy nodules were present as far down as 6 in. below the anterior superior iliac spines. The same phenomenon was witnessed in the right arm, while the distal portions, both of the upper and lower limbs, remained entirely free from nodules, and perfectly smooth to palpation.

The nodules present in this case did not belong to the ordinary type of subcutaneous nodules. A few were situated in the subcutaneous tissue, but most of them lay either on the deep fascia or in the superficial layer of the muscles. It should also be noted that the largest nodules were in the immediate neighbourhood of the growth, and that only these were adherent to the skin. So that nodules presumably made their earliest appearance close to the primary growth. The distribution of the nodules in this case strongly indicates that fascial and muscular nodules obey the same centrifugal law

which, in Chapter II., has been shown to apply to true subcutaneous nodules and to bone metastases.

In order to obtain microscopic evidence for or against the hypothesis put forward above, the following strips of the parietal tissues were removed and examined histologically along their whole length :—

(1) A strip of tissue commencing above at the right acromial process, and passing down the outer side of the arm to a point 6 in. above the wrist.

(2) A coronal strip of the scalp from the vertex to the ear.

(3) A median strip extending on the front of the body from the chin down to the pubes.

The results of the microscopic examination were in this case negative. Numerous isolated nodules were found on the one hand in the subcutaneous tissue, and on the other hand in the muscle. The skin had almost everywhere escaped invasion. No sign of invasion of blood vessels was seen. It could be made out with great probability that the muscles were first invaded on their superficial aspect, for the two youngest isolated foci of cancer seen in the muscle were just beneath the overlying fascia.

At one point a tiny isolated group of cancer cells in the subcutaneous tissue was surrounded by leucocytes. The cancer cells were degenerate, but still clearly recognisable, and the view suggested itself that this focus was being destroyed by phagocytosis.

Having described the five cases in detail, I now propose to give a general account of the processes of permeation, perilymphatic fibrosis, and nodule formation, which appear to be the essential factors in the parietal dissemination of breast cancer. This account is based on the cases I have related.

PERMEATION AND ITS SEQUELS.

The growth of cancer along the lymphatic vessels is, no doubt, simply the result of that same tendency to take the direction of least resistance, which on the surface of the body manifests itself in fungation. By preference the process seems to follow vessels of not less than 40 or 50μ in diameter, avoiding for a time those of smaller calibre, and, therefore,

higher resistance (see Fig. 16). For this reason the parietal growing edge of a breast-cancer follows the plane of the deep fascia where the main lymphatic plexus is situated.

The trunk lymphatics also escape permeation, but for a different reason. In them the lymph stream is strong enough to sweep away as emboli any cancer cells gaining an entrance, until in a late stage their outlet is dammed by growth in the glands, or by external pressure on their walls. This is a sufficient reason for the rarity with which cancer is found in the thoracic duct. Nevertheless, when cancer of the thoracic duct is met with, the duct and its tributaries are often so obviously converted into solid cancerous cords* that the process of permeation can be seen with the naked eye.

For the naked-eye recognition of lymphatic permeation, however, vessels of large size are not absolutely necessary. In favourable situations the process can be seen even in very minute lymphatic vessels.

Cancer cells which escape into the pleural cavity are apt to implant themselves at some point on its surface, and originate pseudo-papillomatous secondary growths. Round such an implantation growth, a roughly circular, opaque, and slightly thickened area of pleura can often be seen, perhaps an inch or two in diameter. Close observation reveals this opaque area as a network of fine white lines, just visible to the unaided sight. The microscope shows these lines to be vessels of the sub-pleural lymphatic plexus filled by cancer cells.

The small implantation growth and the permeated circle of pleura round it may be regarded as a rough model on a small scale of the primary mammary growth and of the surrounding invaded area of the parietal lymphatic plexus.

In certain situations, under the misleading name of *lymphangitis carcinomatosa*, permeation has long been recognised and described. Borst † describes the process in the following terms :—

"A very interesting form of lymph-vessel metastasis is the so-called *lymphangitis carcinomatosa*. One meets with

* See Hillier, "Carcinoma of the Thoracic Duct." Trans. Path. Soc., 1903, p. 153.

† Borst, "Die Lehre von den Geschwülsten," Wiesbaden, 1902, Vol. II., p. 712.

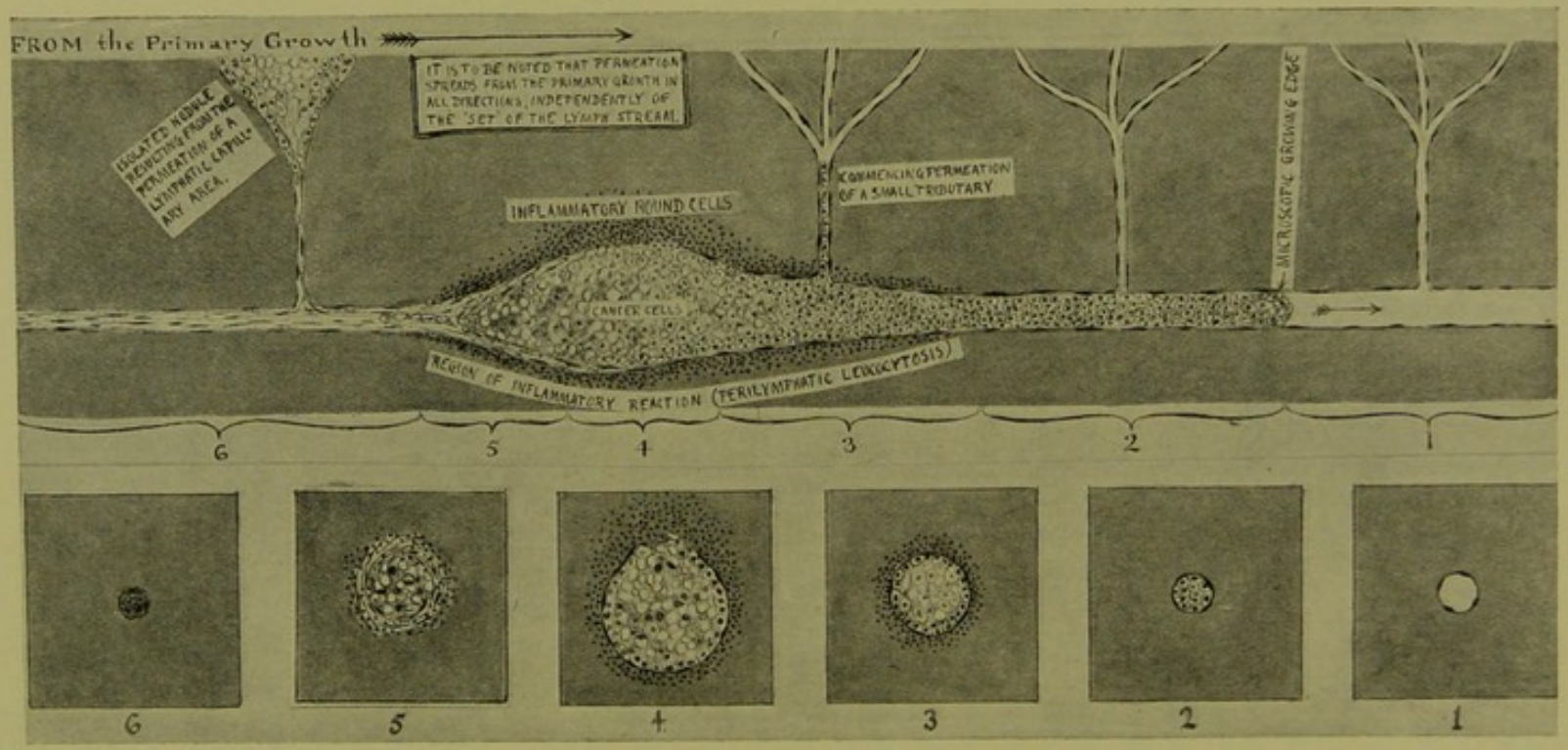
it in the serous membranes, in the diaphragm, in the lungs, and in the liver. All the lymph vessels of the affected region are filled with cancer masses, so that the microscopical appearances not only resemble, but even surpass, an artificial injection of the lymphatic plexus."

It will be seen that Borst regards this process as peculiar to certain organs—that he does not recognise it, for instance, as occurring in the parietal lymphatics, nor describe it as taking any important share in dissemination. It will, I think, ultimately be found that permeation invariably occurs in the lymphatics round all carcinomata which give rise to metastases. It must, however, be admitted that in certain cases, such as Case V., permeation cannot be demonstrated anywhere in the tissues. But a lymphatic along which cancer cells have pushed their way does not persist unchanged, either usually or necessarily, until the patient's death affords an opportunity of observing it. It is in accordance with our knowledge of the reaction of the tissues to other foreign bodies that a process of fibrosis should occur round the permeated lymphatic and should usually succeed in destroying the slender cylinder of cancer cells within.

Indications of the nature of this process have already been given, but it must now be studied more in detail. For convenience of reference I have called the process "Perilymphatic Fibrosis."

Perilymphatic Fibrosis.—M. B. Schmidt has shown that in a blood vessel cancer cells excite an organising thrombosis which usually ends in their destruction. So far as I have seen the lymph exhibits no such thrombotic reaction to cancerous invasion. Nor in the tissues around a permeated lymphatic is there at first any sign of inflammatory reaction.

Soon, however, the elastic tube in which the cancer cells lie is stretched by their proliferation to several times its normal diameter, and there ensues a process of inflammatory fibrosis around the vessel, analogous to that which on a large scale follows the prolonged distension of a hollow viscus such as the gall-bladder. The commencement of this process is heralded by the appearance of small round cells in the perilymphatic tissues.



Cf. Fig. 23. Cf. Fig. 22. Cf. Fig. 20. Cf. Fig. 19. Cf. Fig. 15.

FIG. 12.

Scheme to illustrate the advance of permeation along a small lymphatic, seen in the upper figure in longitudinal section, and in the lower figures as a series of transverse sections. The lymphatic is finally destroyed by perilymphatic fibrosis. 1. Normal lymphatic, shortly to be invaded by the advance of permeation along it. 2. Lymphatic permeated by cancer cells, but not yet distended. Note the absence of inflammatory reaction in this region. 3. The lymphatic distended by the growing cancer cells. The central cancer cells are becoming degenerate. 4. The lymphatic ruptured by the growing cancer cells, an event followed by vigorous inflammatory reaction. 5. The mass of degenerate cancer cells enclosed in a false capsule of newly formed fibrous tissue. 6. The cancer cells are finally strangled by contraction of their fibrous capsule. The original lymphatic is now represented simply by a thread of fibrous tissue, the cancer cells having been destroyed. (For photomicrographs of the various stages of this process, see Figs. 15 to 23.)

In the course of time the hyper-distended lymphatic bursts, and slight traumatic hæmorrhage often occurs in consequence around the enclosed group of cancer cells. The cylinder of cancerous epithelium thus released from pressure is now apparently free to invade the adjoining tissues. But the inflammatory reaction already present is greatly intensified by the rupture of the lymphatic. Abundant round-celled exudation takes place. Soon granulation tissue takes the place of round cells, and forms a definite new capsule for the cancer cells. The further organisation of this granulation tissue into fibrous tissue is accompanied by shrinkage of the fibrous capsule, which contracts upon and slowly strangles the remaining cancer cells. Ultimately the original permeated lymphatic is replaced by a slender cord of fibrous tissue in which no cancer cells can be seen. (Figs. 15 to 23.)

That the rupture of a permeated lymphatic does not invariably lead to local invasion of the surrounding tissues, depends also upon the point that the cancer cells set free are often incapable of growth. The proliferating cancer cells within a lymphatic are themselves subject to the same harmful pressure which they exert upon its walls. The effects of this pressure are often to be seen in their swollen, degenerate, and unstained character. Frequently only the layer of cells abutting immediately on the endothelium preserves the appearances of vitality. So that when the cancer cells rupture the lymphatic and are free to invade the tissues, they are neither numerous enough nor sufficiently vigorous to withstand the traumatic inflammatory reaction which follows.

As a curative process perilymphatic fibrosis has unfortunately certain defects. In the first place it does not follow permeation with sufficient promptness to overtake the microscopic growing edge where permeation is just beginning.* In the second place, the contraction of the perilymphatic fibrous tissue helps to force cancer cells along the smaller tributary lymphatics, which on account of their higher resistance have hitherto escaped invasion. Passing along these vessels the cancer cells reach and permeate the bundle

* Cf. Lazarus-Barlow on Stroma-formation. "Textbook of General or Experimental Pathology," 2nd Edition, p. 515.

of lymphatic capillaries from which each of the small lymphatic vessels arises. The wall of these lymphatic capillaries consists merely of endothelium, and is quite unfitted to resist a pressure such as growing cancer cells can exert. Before an adequate inflammatory reaction can ensue the cancer cells rupture the lymphatic capillaries and invade the surrounding tissues. If, therefore, living cancer cells in this way reach the extreme periphery of the lymphatic system, they are able to originate metastases. Such metastases are often sharply circumscribed nodules, a form which may be determined, according to my observations, by extension of cancerous growth along all the lymphatic capillaries which drain into some one lymphatic. In its early stages the nodule maps out the limits of this capillary lymphatic area.

The metastases which thus arise in the various layers of the parietes, though apparently discrete and sporadic, are genetically continuous with the primary growth. But perilymphatic fibrosis has destroyed the evidence of their continuity with it.

It should be especially noted that in their earliest stages the processes I have described are only to be seen at the microscopic growing edge, and that as one passes towards the primary growth they become visible in more and more advanced stages. Thus, as might be expected, all these stages may be recognised in a single favourable radial section of the primary growth extending to its microscopic growing edge. To trace the course of events along the length of a single lymphatic is naturally most difficult. But Figs. 22 and 23, showing the middle and the penultimate stages of fibrosis, are derived from a fortunate series of sections of the same lymphatic at different points along its length.

THE ZONAL ARRANGEMENT OF BREAST CANCER IN THE PARIETES.

It will be seen that the parietal metastases, except the embolic ones, which probably occur only in the lymphatic glands, are really parts of the primary growth. The expression "primary growth" may, however, be defined as the region of interstitial infiltration round the original primary

focus. As thus defined the primary growth is surrounded by three zones:—

(1) The zone of isolated or confluent nodules in which the permeated lymphatics have been destroyed.

(2) The zone in which perilymphatic fibrosis is actively progressing, and in which nodule-formation on either side of the main lymphatic plexus is seen in an early stage.

(3) The zone of fascial permeation. This is subdivisible into a proximal zone characterised by distension and rupture of the lymphatics, and by perilymphatic leucocytosis, and a peripheral zone in which distension of the lymphatics has hardly commenced, and in which therefore no inflammatory reaction has yet taken place.

Even the negative results of Case V., which cannot in any case outweigh the positive evidence of Cases I. to IV., are best explained by the theory of permeation. I am not aware of any theory but that of permeation which will explain the centrifugal extension so clearly manifested in this case by the clinical evidence. And as regards the microscopical evidence it is at least possible that the strips examined, long though they were, failed to pass beyond the zone of isolated nodules into the outlying zones of active fibrosis and of permeation.

The Origin of Subcutaneous Nodules.

(See Figs. 24–26, Plates VI. and VII.)

In Chapter II. reasons not in themselves conclusive were given for believing that subcutaneous nodules are "efflorescences" from the subjacent permeated lymphatic plexus of the deep fascia, and that they do not indicate the spread of cancer in the plane of the skin. In Chapter III. this view was further supported by reference to the lymphatic anatomy of the parietes. The microscopic evidence just adduced fully establishes it. It has been shown that cancer in the skin makes its appearance in the form of isolated nodules, between which there appears to be no connexion. Invasion of the deep fascia on the contrary occurs by the growth of cancer in continuity along the fascial lymphatic plexus, and is moreover usually much more extensive than invasion of the skin

(cf. Fig. 13), except in cases (Fig. 14) where the cancer is extending very slowly.

Subcutaneous nodules arise by the up-stream extension of permeation from the permeated fascial plexus along its cutaneous tributaries, and thence into the network of fine cutaneous lymphatics from which each of these tributaries arises. In fortunate sections the earliest stage of this process may be traced. (Fig. 24.)

Contraction of the Tissues around a Carcinoma.

One of the most marked clinical features of carcinoma is the strong tendency to contraction which the growth exhibits. The phenomenon is not limited to the primary growth itself, but involves also a considerable area of the surrounding apparently healthy tissues. In breast-cancer retraction of the nipple is one of the earliest manifestations of this tendency. The affected breast is often smaller than its fellow, and is, moreover, situated on a higher level because it is dragged towards, and fixed to, the pectoral fascia. All these events may occur while yet the primary growth is but a small lump in the breast.

Shrinkage of the primary growth is ascribed, rightly no doubt, to the contraction of its stroma; but the tendency of a carcinoma to drag in towards itself the surrounding apparently healthy tissues from all sides has never received a clear or adequate explanation. It is, in fact, an inevitable sequel of the process of perilymphatic fibrosis. If over a wide area around the growth the normal network of lymphatic vessels is replaced by a network of threads of newly-formed, and therefore contractile, fibrous tissue, a general puckering and shrinkage of the affected zone is likely to follow.

Variability of the Rate of Spread of Permeation.

I have deliberately confined my investigations on permeation to late cases in which the patient has died of the disease, and to the region around the breast. The only practicable alternative to this course is to examine breasts excised by operation from the living subject, a line of research

which has already, with most valuable results, been followed up by Stiles to the limits of its usefulness. The defects of the method are that the relations of the specimen are disturbed and dislocated, especially at its thin margin; that in all probability the plugs of cancer cells filling the lymphatics are frequently squeezed out; and that it is generally impossible within the anatomical limits of the specimen to prove conclusively by the examination of a wide peripheral margin of normal tissue that the microscopic growing edge of the carcinoma has been reached. Moreover the large scale of the mammary gland, and the complexity of its normal structure, confuse and complicate any investigation into the mode of spread of cancer within it.

In the circum-mammary region on the other hand, where the lymphatic system is relatively simple, and where the various layers of the parietes, in thin subjects, can all be included in the area of one microscopic section, it is possible to trace the processes of dissemination in orderly sequence.

It is quite erroneous to imply, as some of my critics have done, that the investigation of late cases can only elicit facts of purely pathological import, with no practical bearing on surgery. That fascial permeation commences early is shown by Heidenhain's researches, for he found cancer-filled lymphatics running from the breast to the pectoral fascia in ten out of fifteen excised breasts. I have confirmed the statement that permeated lymphatics may be found in the pectoral fascia before the mamma has become adherent to it. There is thus strong evidence that fascial permeation commences a considerable time before the case ceases to be operable, and while in certain cases the spread of permeation is doubtless slow and limited, it appears equally certain, especially from the comparison of operative results given on page 45, that in other cases—cases still coming within the operable category—the circle of permeation will already at the time of operation have attained a considerable diameter.

Owing to the great variations in the rapidity of spread of fascial permeation, the area of permeation found in one case post mortem may in another and more rapid case be attained or exceeded in an early stage, at the time the case is operated upon.

The Explanation of Cases of Late Recurrence.

It is possible that in some cases the microscopic growing edge may die out along one portion of its circumference, and that the remaining portion, like some tertiary syphilides, may continue to advance as an arc of a circle. It is probable that not infrequently permeation may smoulder along the lymphatics without giving rise to macroscopic nodules in its course. In such cases long periods of apparent immunity may be followed by recrudescence of the growth at some distant point, towards which in the meantime the process of permeation has steadily been creeping in a latent and microscopic form. A rational explanation is thus afforded of the unsolved mystery of recurrence after many years of quiescence and apparent cure.

Centrifugal Permeation in its Practical Aspects.

The facts detailed in the foregoing chapter evidently supply a basis upon which to build operative methods. Unfortunately the microscopic growing edge is not clinically recognisable, and the surgeon cannot determine for each case as it comes before him how far the circle of fascial Permeation has extended. If the case is a very early one, permeation may still be confined entirely within the limits of the breast. If it is moderately early, only a small area of the pectoral lymphatic plexus, an area perhaps not so large as the diameter of the breast, may have been invaded. But if the case, though still operable, is late, or if the cancerous epithelium is proliferating with more than average rapidity, the permeated area of the deep fascial plexus may already have passed considerably beyond the margin of the breast.

Since there are no satisfactory clinical means at present of fixing the limit of fascial permeation in a given case, the only safe rule is to remove a very wide circle of the deep fascia round the growth, and a smaller circular area of skin.

The discussion of operative methods is reserved for another chapter.

Summary of Conclusions.

Dissemination is usually accomplished by the actual growth of cancer cells along the finer vessels of the lymphatic plexuses—"permeation." Embolic invasion of the regional lymphatic glands, though it almost invariably occurs, only leads to invasion of the blood-stream after long delay; and the work of M. B. Schmidt shows that cancer cells which reach the blood usually disappear without giving rise to metastases.

Permeation takes place almost as readily against the lymph-stream as with it. It spreads through the lymphatic vessels around the primary neoplasm in much the same way as would a thick injection fluid introduced into the tissues by a syringe. If in a late case of breast cancer one examines the region immediately around the macroscopic primary growth, no permeated lymphatics can be detected. Here and there are secondary nodules of growth entirely isolated from one another and from the primary neoplasm.

If, however, the investigation is pushed still further from the primary growth, by the examination of long radial sections of the skin and underlying tissues, we arrive at a region beyond the remotest visible naked eye metastasis and often lying far from the primary growth. In this region the microscopic growing edge of the carcinoma will usually be detected by careful microscopic search. The microscopic growing edge is to be sharply distinguished from the infiltrating edge of the primary neoplasm where interstitial invasion of the surrounding tissues is occurring. At the peripheral microscopic growing edge there is no interstitial invasion of the tissues, but the principal lymphatic plexus of the part—the plexus which lies upon the deep fascia—is found permeated throughout—that is to say, its vessels are obstructed by the growth of lines of cancer cells along them.

The disappearance of permeated lymphatics in the area which intervenes between the annular "microscopic growing edge" and the primary neoplasm is due to the destruction, after a time, of the cancerous permeated lymphatics by the defensive process of "perilymphatic fibrosis." The recognition of this process at once removes the difficulty that permeated

lymphatics are absent in the region immediately surrounding the naked eye primary growth.

The process of permeation follows the line of least resistance, and extends, at first exclusively, in the plane of the principal lymphatic plexus into which the lymph drainage of the cancerous organ passes. The annular microscopic growing edge of a breast cancer is therefore found in the plane of the fascial lymphatic plexus, upon, or just superficial to, the deep fascia. It is covered over by normal skin and has lying beneath it normal muscles.

If, however, the tissues are examined at points successively intermediate between the microscopic growing edge and the apparent edge of the primary growth, the cancer will be found penetrating the adjoining layers, the superjacent skin and the subjacent muscle, to a greater and greater depth, and forming nodular deposits therein, which may, however, be sporadic and few in number, and in some cases may be altogether absent.

Cancer thus spreads in the parietal tissues by permeating the lymphatic system like an invisible annular ringworm. The growing edge extends like a ripple, in a wider and wider circle, within whose circumference healing processes take place, so that the area of permeation at any one time is not a disc but a ring. The spread of cancer in the parietal tissues is, in fact as truly a serpiginous process as the most typical tertiary syphilide. But in the case of cancer the spreading edge is invisible; and, moreover, the advancing microscopic growing edge of a cancer, owing to the failure at isolated points of the defensive process of perilymphatic fibrosis, may leave in its track, here and there, isolated secondary foci, which give rise to macroscopic metastases. Such nodules, in spite of their apparent isolation, arise in continuity with the primary growth, but perilymphatic fibrosis has destroyed the permeated lymphatics which formed the lines of communication.

Note.—In connection with this chapter, the reader is asked to read the Appendix (p. 203), and especially to study Fig. 47, p. 208.

DESCRIPTION OF FIGURES (Plates I.–IX.).

FIG. 13, from Case I. shows the parietal edge of a breast cancer of moderately rapid growth. It is a nearly median section of the parietes in the sagittal plane taken from the epigastric region of the abdomen just below the ensiform cartilage. On the left is seen the skin surface, and to the extreme right a superficial layer of the rectus muscle. Immediately overlying the rectus muscle is the anterior layer of its sheath. In the whole length of the drawing the foci of growth are confined to the surface of the rectus sheath and to the deeper layer of the subcutaneous tissue. Opposite each focus of growth, along the left of the figure, is a numeral indicating its level in mm. above the umbilicus, and referring to the detailed description of Case I. The skin and muscle are entirely free from growth, though in the region above the figure, i.e., nearer to the primary growth, nodules were found in both these layers.

The figure shows the whole width of the "zone of fascial permeation."

FIG. 14 (× 25), from Case II. Strip A, shows the parietal edge of a breast cancer of slow growth. Above is seen the skin surface, while at the lower edge is a layer of muscle.

In the fascial layer, along the line A B C, a number of lymphatics are seen in longitudinal section. They are permeated, but not distended, by cancer cells. Fig. 17 shows one of these lymphatics highly magnified. At the point C is the actual growing edge of the cancer in the fascia. In this particular section the skin is invaded about ·3 mm. beyond the fascia. The remotest subcutaneous nodule is seen at G. This nodule is connected with a proximal point in the deep fascia by a fibrous septum D E F, which runs very obliquely in a distal direction. The figure shows the distal part of the "zone of fascial permeation."

FIGS. 15 TO 23.—THE VARIOUS STAGES OF PERMEATION AND OF PERILYMPHATIC FIBROSIS.

Zone of Permeation without Inflammatory Reaction.

FIG. 15 (× 90).—From the abdominal wall, 160 mm. above the umbilicus, at the extreme growing edge in Case I. (see Fig. 13). Crossing the lower half of the field is the anterior layer of the rectus sheath. Upon its superficial aspect are seen in transverse section two lymphatics filled by cancer cells. Between them is a normal blood vessel. Note the absence of perilymphatic leucocytosis.

FIG. 16 (× 60).—A similar section taken from Fig. 13. A permeated lymphatic is seen in transverse section. Running from it through the anterior layer of the rectus sheath, and bifurcating on its deep aspect, is a small branch lymphatic, along which permeation has not yet extended.

[To illustrate the proposition that permeation follows the line of least resistance avoiding for a time the smaller lymphatics. Hence the growing edge of a breast cancer is situated in the deep fascia, in the plane of the principal parietal lymphatic plexus.]

FIG. 17 (× 120).—A highly magnified portion of Fig. 14, from the growing edge in Case II., Strip A. The figure shows a permeated lymphatic in longitudinal section. The lymphatic endothelium is clearly visible. Above and below the lymphatic are seen normal blood vessels, also cut longitudinally. The lower one is bifurcating.

[This figure shows that the groups of cancer cells seen in Figs. 15 and 16 are sections of cylinders, not isolated clumps of cells.]

Zone of Permeation with Perilymphatic Leucocytosis.

FIG. 18 (× 96).—A highly magnified portion of Fig. 13. The anterior layer of the Rectus sheath crosses the lower half of the field. The permeated lymphatic visible is beginning to be distended from proliferation of the cancer cells within it. A few emigrated leucocytes are present near an adjacent normal blood vessel. The cancer cells have not yet suffered any injury from the increased intra-lymphatic pressure.

FIG. 19 (× 100).—From Case I. A transversely-cut permeated lymphatic greatly distended by the proliferation of the cancer cells within it. The nuclei of the lymphatic endothelium are consequently only seen at wide intervals. The cancer cells, except the layer next the endothelium, have suffered from pressure, and are swollen, hyaline, degenerate and polygonal. There is moderate peri-lymphatic leucocytosis.

FIG. 20 (× 72).—From the muscular layer in Case I. The limit of the resistance to distension offered by the wall of the lymphatic has been reached, and the tube has split along one side, but not before, as a result of the increased intra-lymphatic pressure, cancer cells have grown along the small branch lymphatics seen in the upper part of the figure. The rupture of the lymphatic has caused slight hæmorrhage and has much increased the pre-existing leucocytosis. Clearly, therefore, the rupture was an ante-mortem event. This is further shown by the degenerative changes which the extravasated red corpuscles have undergone.

(In Fig. 13 at levels 182·9, 184·5, 186, and 188·3 mm., rupture of lymphatics is also traceable, but in a less recent and unequivocal form.)

Zone of Active Perilymphatic Fibrosis, with early Nodule Formation.

FIG. 21 (× 100).—From Case I. The degenerate cancer cells set free by rupture of the lymphatic are enveloped in a fibrous area infiltrated by round cells, and appear to be in process of destruction.

(The subsequent stages of fibrosis were obscured in Case I. by the abundant formation of nodules which occurred, but they were traced in Case II. along the length of the same lymphatic.)

FIG. 22 (× 45).—From Case II., Strip B. The mass of degenerate cancer cells set free from the ruptured lymphatic is now enclosed in a definite capsule of newly-formed fibrous tissue, in which many leucocytes are still visible. Normal blood vessels are seen at the edge of the field.

FIG. 23 (× 180).—The penultimate stage of perilymphatic fibrosis. A section at another part of its course of the fibrosed lymphatic seen in Fig. 22. To show the characters of the newly-formed fibrous tissue Fig. 23 is much more highly magnified than Fig. 22.

The fibrosed lymphatic has shrunk to about half its diameter. A few cancer cells in the last stages of destruction still persist as islets in the contracting fibrous tissue. Round cells have given place to the fusiform cells of young fibrous tissue, and newly formed capillaries are visible here and there in the fibrous area.

The Formation of Subcutaneous Nodules.

Fig. 24.—The first step towards the formation of a subcutaneous nodule. The figure shows the deeper layer of the subcutaneous fat traversed vertically by one of the fibrous septa which unite the skin with the deep fascia. These septa carry the lymphatics from the skin. From a small cancer-nodule which lies upon the deep fascia permeation is seen extending towards the skin along a minute lymphatic lined by definite endothelium which happens to lie for some distance in the plane of the section.

FIG. 25 (× 20).—From the proximal portion of Strip B, Case II. Above is seen the deepest layer of the dermis, densely infiltrated by cancer, while close to the lower margin of the field, above and to the left of a normal blood-vessel, is a fibrosed lymphatic lying upon the fascial layer which here crosses the figure transversely. The deep fascia in this region is for the most part free from cancer and only here and there still shows obsolescent foci of cancer like the one represented.

The two conical sub-dermal areas of cancerous infiltration are formed by the extension of permeation along the bundle of small lymphatics which by their union form a vertical tributary of the fascial plexus. From the area on the right of the figure a distinct "tail," consisting of a permeated vertical tributary not yet fibrosed along its whole length can be followed for some distance towards the fascia.

FIG. 26 (× 60).—A high-power photograph of the fibrosed lymphatic seen on the fascia in Fig, 25. Cf. Fig. 23.

The Formation of Nodules in Muscle.

The stage preceding nodule formation can be studied in Fig. 20, where cancer cells are extending along the small tributaries of a permeated and ruptured muscular lymphatic.

FIG. 27 (× 100) shows permeation extending to the extreme periphery of the lymphatic system. The lymphatics of origin among the muscular bundles are mapped out as an arborescent figure, with a main horizontally running branch and vertical side branches. The muscle fibres are still normal, and the permeated lymphatics are not fibrosed.

FIG. 28 (× 150).—The next stage in the formation of muscular nodules. The cancer cells are invading and have partially replaced the muscle fibres themselves, while the permeated lymphatics are undergoing fibrosis, and will ultimately form part of the stroma. A partially fibrosed lymphatic runs horizontally across the centre of the field.

FIG. 29 (× 20).—Below and to the right is seen the edge of a fully formed muscular nodule which appears darker than the normal muscle occupying the greater portion of the field. Crossing the upper part of the field, nearly horizontally, is the plane of separation between muscle and deep fascia. On the extreme right of the field, close to its upper margin, is a permeated fascial lymphatic undergoing fibrosis. Running vertically down to the cancer nodule from the deep fascia in the vertical plane which bisects the field is a fibrous septum containing a permeated and ruptured lymphatic. The cancer nodule was apparently formed by the extension of permeation into the "catchment area" of this lymphatic.

PLATE I.—THE MICROSCOPIC GROWING EDGE OF A BREAST CANCER (CASE I.).

From the epigastric region of the abdomen.

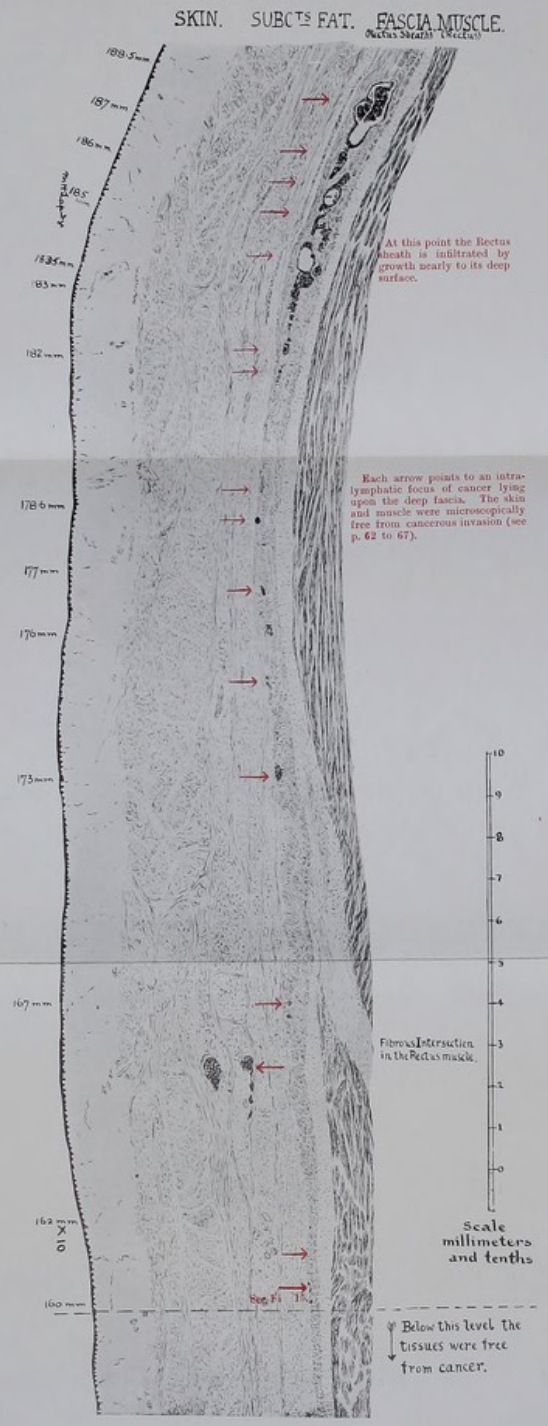
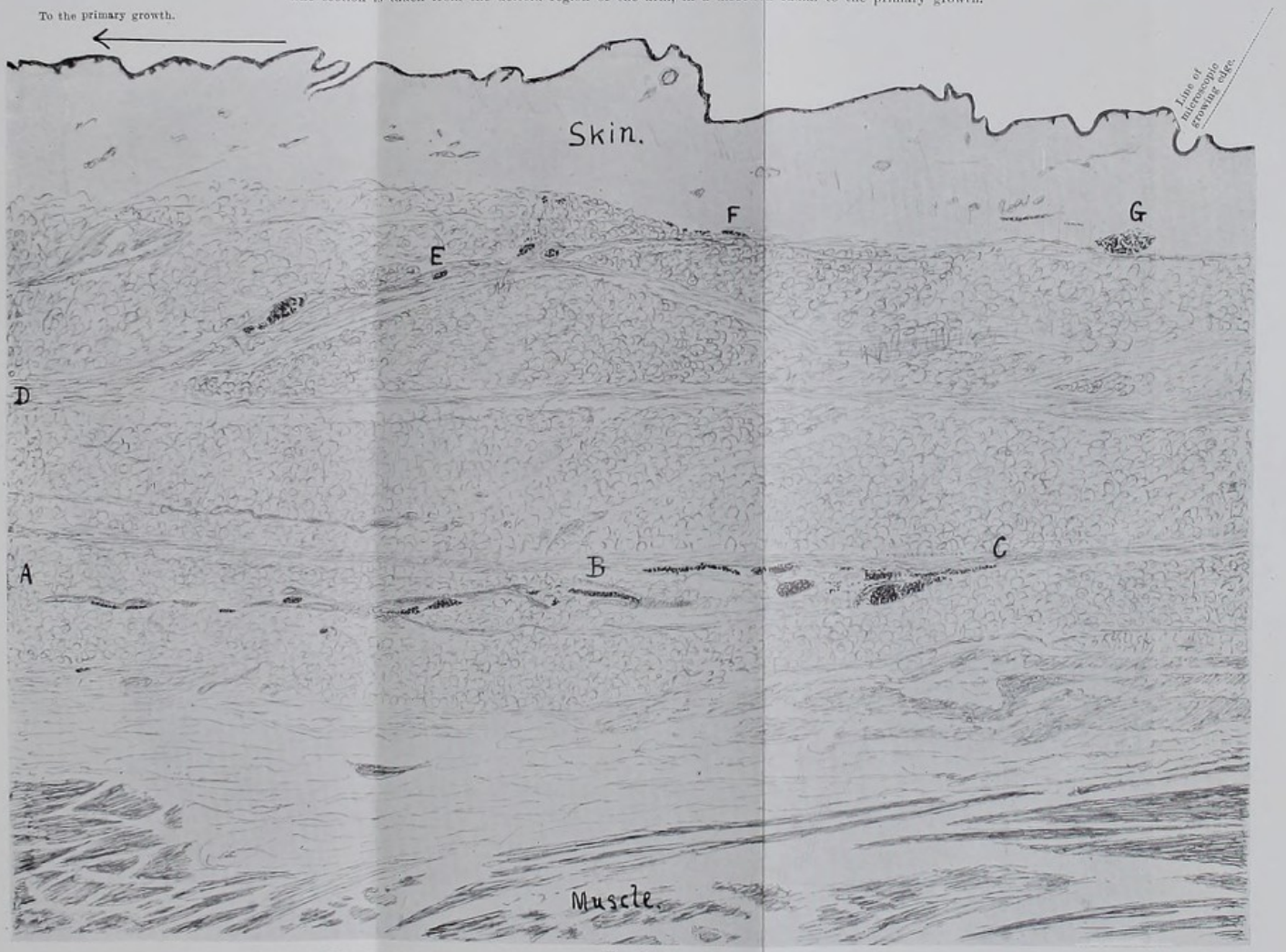


Fig. 13.

PLATE II.—THE MICROSCOPIC GROWING EDGE OF A BREAST CANCER (Case II.).

The section is taken from the deltoid region of the arm, in a direction radial to the primary growth.



Scale of Millimetres and Tenths.

Fig. 14.

PLATE III.—PERMEATION—EARLIEST STAGE.

As seen in the lymphatics close to the microscopic growing edge. There is no distension of the lymphatics, and no inflammatory reaction. In Figs. 15 and 16 the permeated lymphatics are seen in transverse section; in Fig. 17 in longitudinal section.

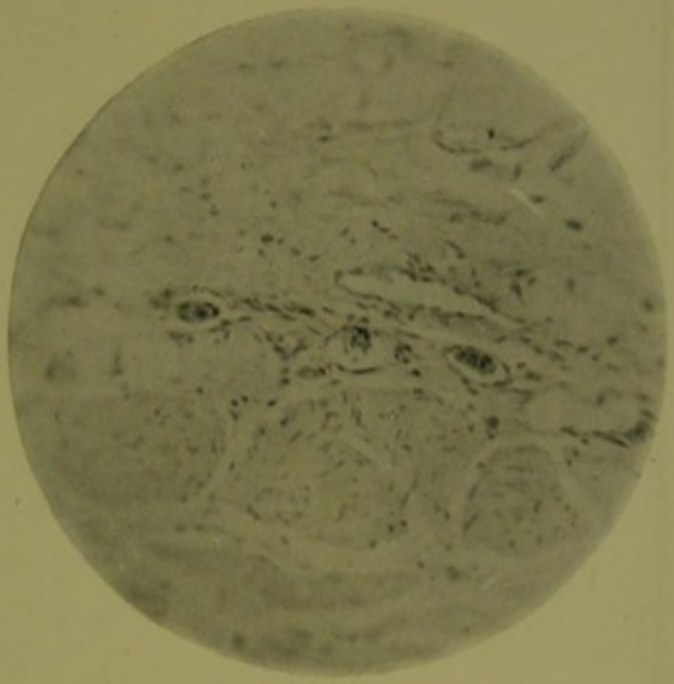


Fig. 15.

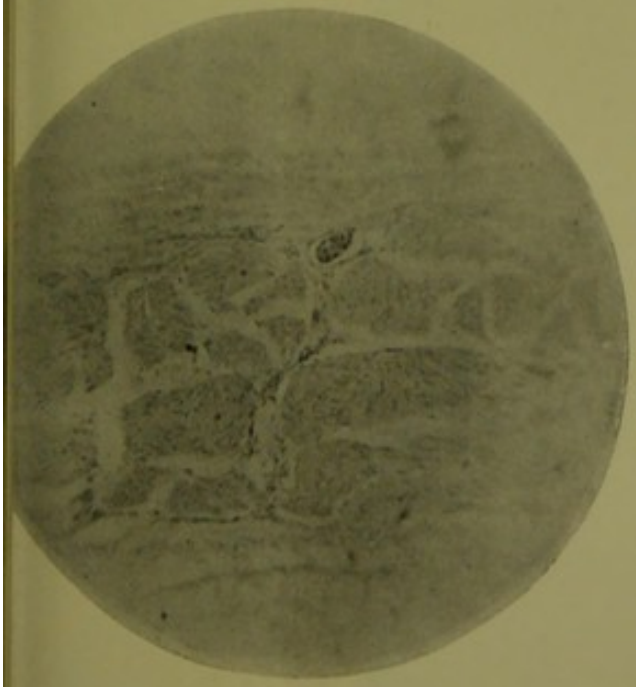


Fig. 16.

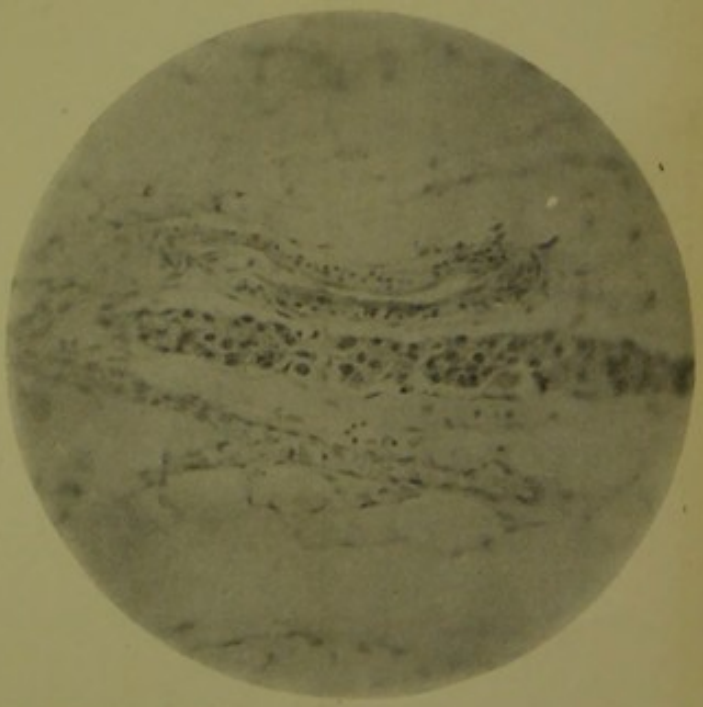


Fig. 17.

PLATE IV.—THE GRADUAL DISTENSION AND RUPTURE OF PERMEATED LYMPHATICS.

The growing cancer cells stretch and finally rupture the lymphatic, and an inflammatory reaction is thus set up.

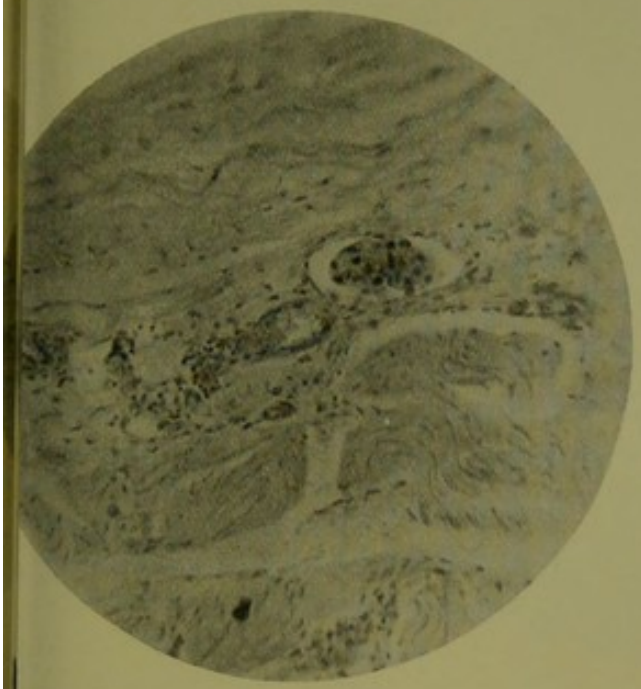


Fig. 18.

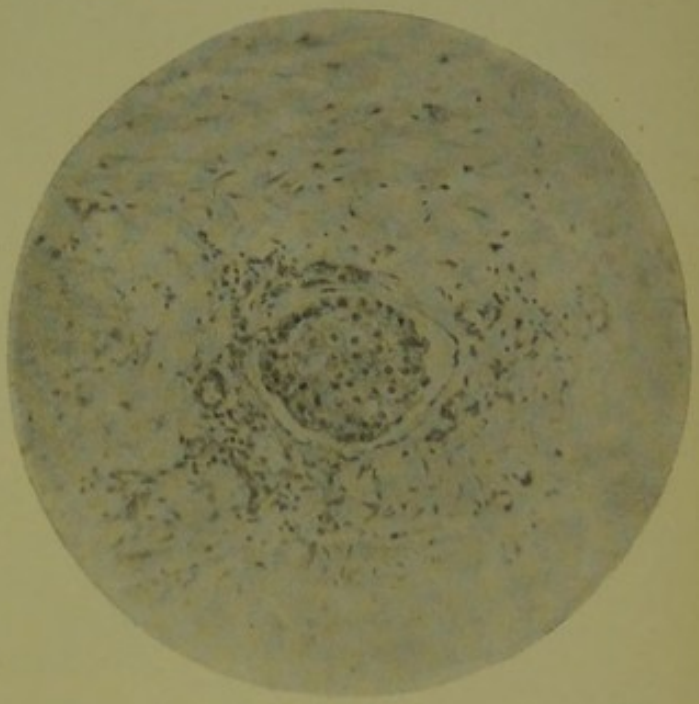


Fig. 19.

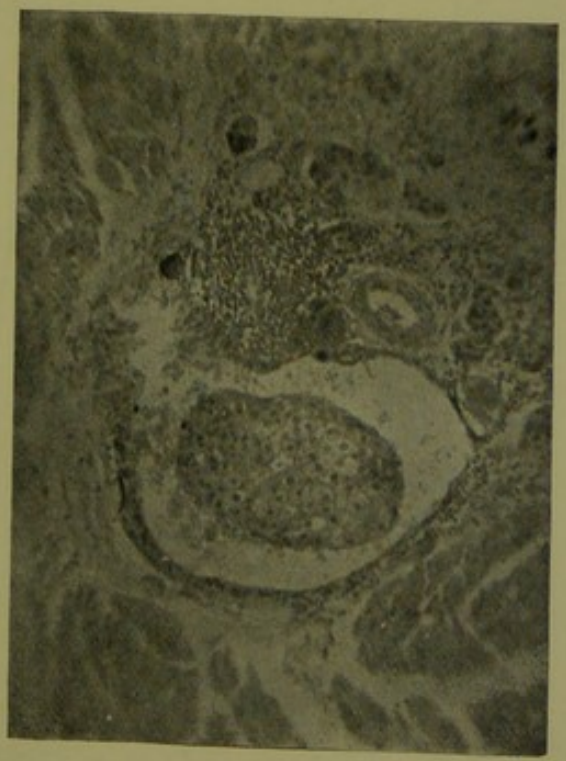


Fig. 20.

PLATE V.—THE DESTRUCTION OF PERMEATED LYMPHATICS BY PERILYMPHATIC FIBROSIS.

The original lymphatic is finally replaced by a thread of newly-formed fibrous tissue, from which cancer-cells have entirely disappeared.

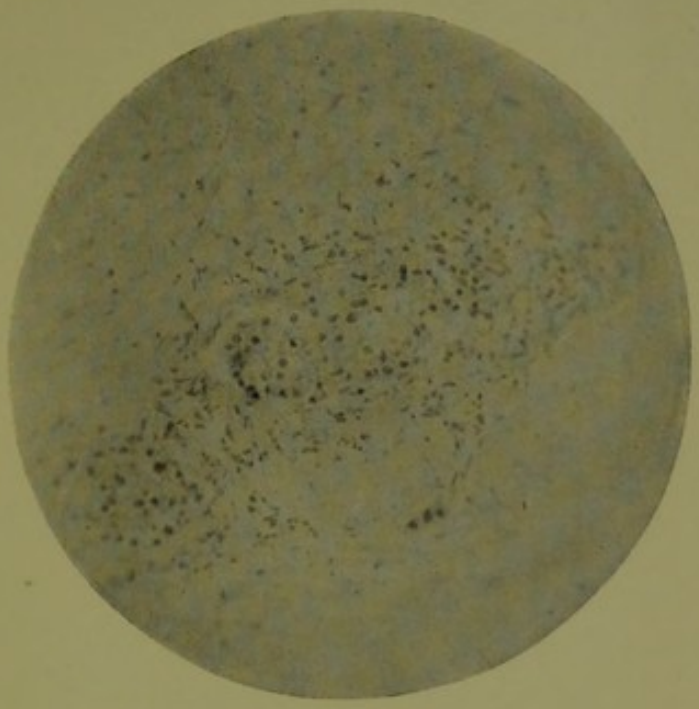


Fig. 21.

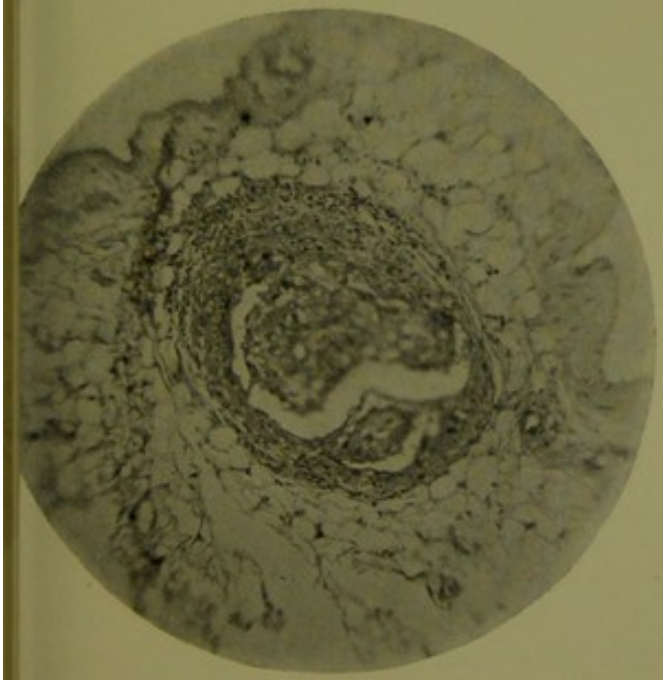


Fig. 22.

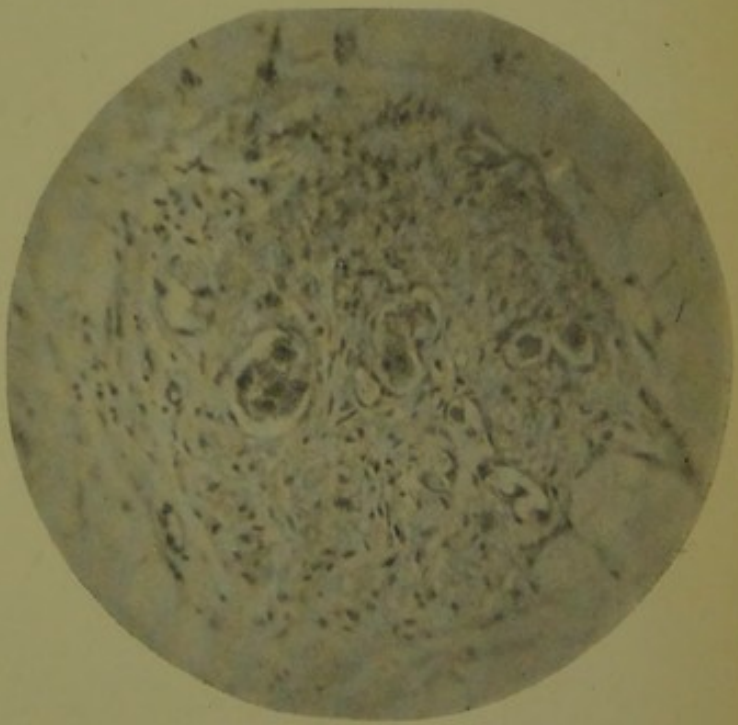
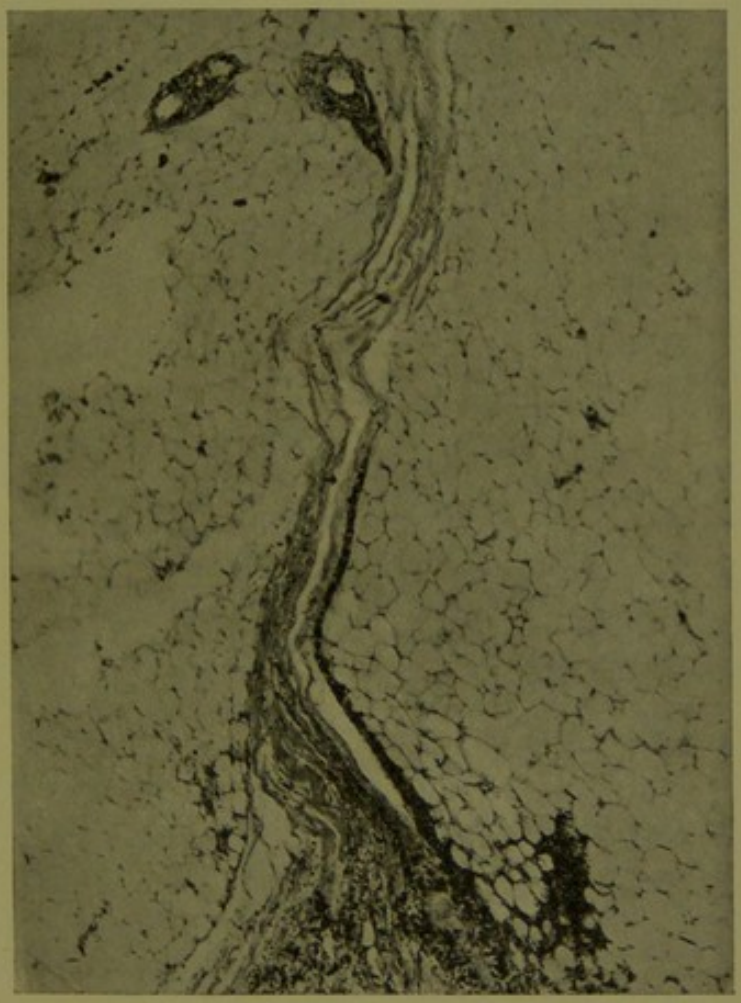


Fig. 23.

(Figs. 22 and 23 are transverse sections of the same lymphatic at points some distance apart. Fig. 23 is much more highly magnified than Fig. 22.)

PLATE VI.—THE FIRST STEP TOWARDS THE FORMATION OF A SUBCUTANEOUS NODULE.



Fibrous septum traversing the subcutaneous fat and carrying a lymphatic, along which permeation is seen extending from the deep fascia towards the skin.

Level of skin surface.

Subcutaneous fat.

Edge of small cancer nodule on the deep fascia.

Level of deep fascia.

Fig. 24.

PLATE VII.—THE FORMATION OF SUBCUTANEOUS NODULES

by the up-stream extension of permeation from the fascial lymphatic plexus along its cutaneous tributaries.

Fig. 25.

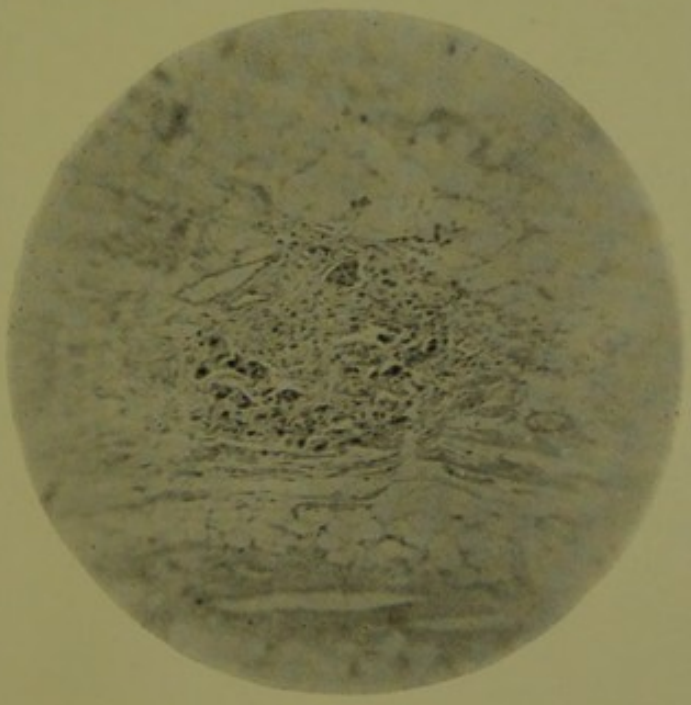


Fig. 26.

PLATE VIII.—THE FORMATION OF MUSCULAR NODULES

by the up-stream extension of permeation along the muscular tributaries of the fascial lymphatic plexus.

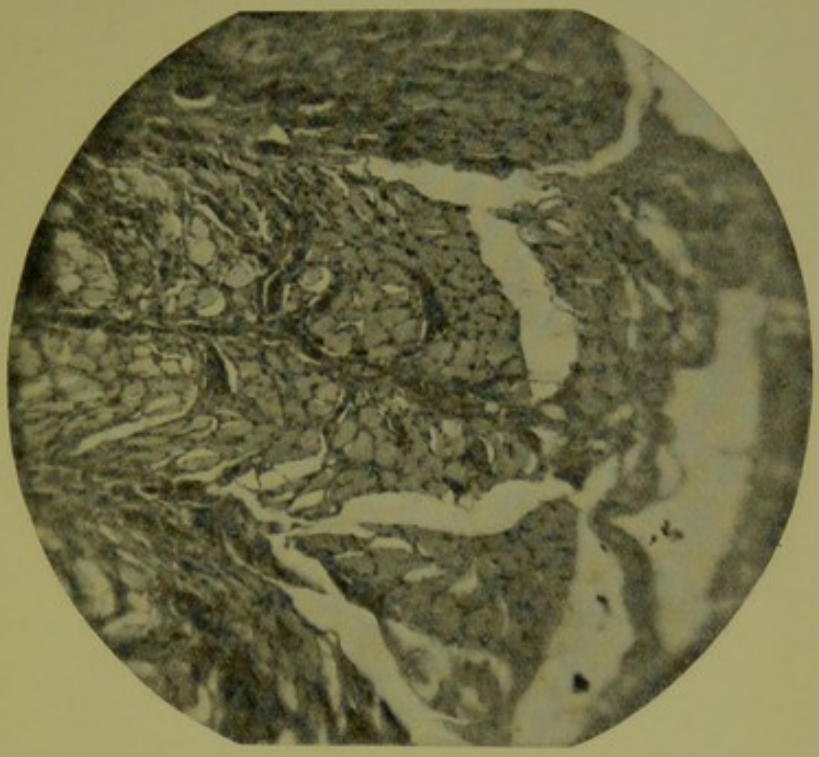


Fig. 27.

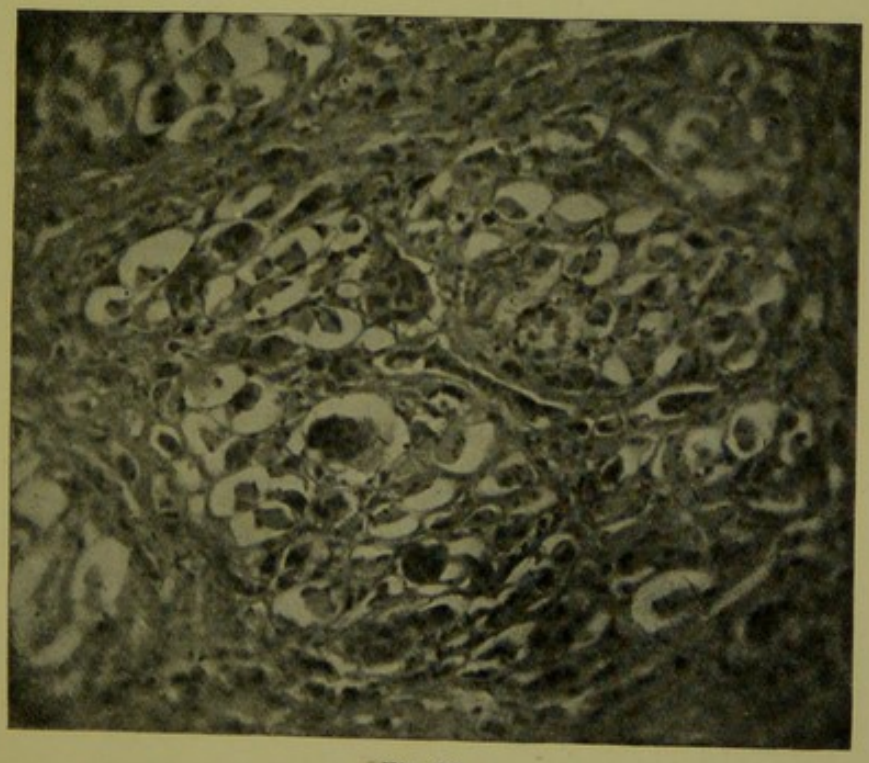


Fig. 28.

PLATE IX.—THE FORMATION OF NODULES IN MUSCLE—LATE STAGE.

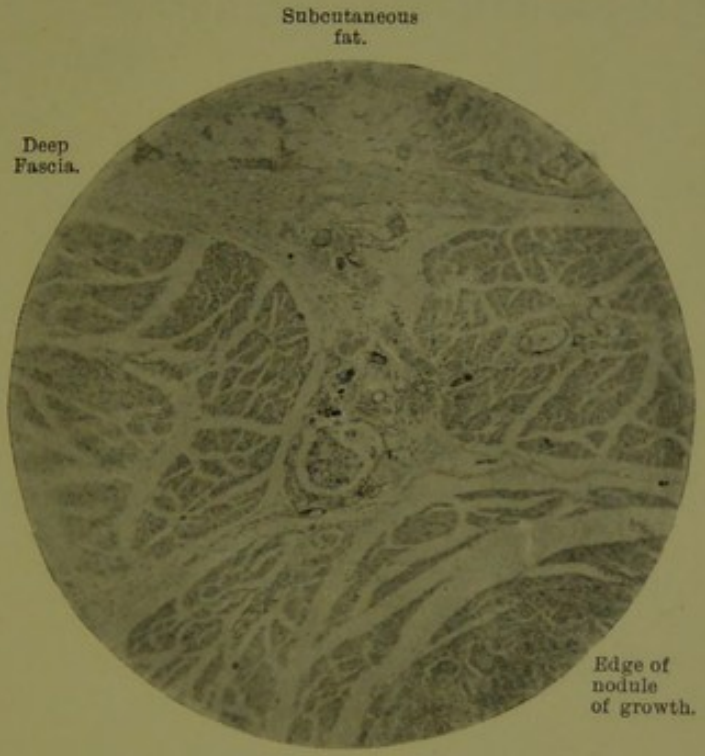


Fig. 29.

CHAPTER V.

VISCERAL DISSEMINATION: A MICROSCOPIC STUDY OF EPIGASTRIC INVASION OF THE ABDOMEN.

Visceral Dissemination.

It may at first sight appear unnecessary to consider visceral dissemination in a work which deals with the pathology of breast cancer mainly from the standpoint of surgical treatment, for when once secondary deposits have formed in the viscera, the case, so far as present knowledge goes, is hopeless. Hence it is, no doubt, that so little attention has been devoted to the subject, and that in most surgical text-books "systemic" dissemination is dismissed in a single vague sentence as explained by the embolic theory.

In reality, however, it is of the highest practical importance to find out how cancer reaches the interior of the thorax and of the abdomen, in order to anticipate a catastrophe, which though irremediable may in certain cases be prevented by timely operative measures.

Summary of Conclusions on Visceral Dissemination.

I shall begin by a frankly dogmatic statement of the conclusions to which a careful study of the subject has led me. The reader will thus be placed from the outset in a position to criticise the evidence subsequently laid before him.

The visceral metastases in breast cancer mainly arise from the extension of cancerous permeation along the numerous fine anastomoses which, piercing the parietes, connect the lymphatic plexus of the deep fascia with the sub-endothelial lymphatic plexuses of the pleura and peritoneum, and with the mediastinal and portal glands. It has already been shown that in parietal dissemination the

main factor is centrifugal permeation of the fascial plexus. And in visceral dissemination, too, permeation, especially of the subserous plexuses, plays an essential part. But these plexuses lie close to the serous surface, and consequently, in the later stages of visceral dissemination, a factor even more important than permeation comes into play. The dominant factor in visceral dissemination is the escape of cancer cells into the serous cavities, their distribution through those cavities under the influence of gravity and of visceral movement, and their implantation at various points upon the serous surface of the viscera. This process may be spoken of as transperitoneal or transpleural implantation. The occurrence of permeation and of embolic gland invasion from each of the foci thus arising, soon terminates the patient's existence.

If this outline sketch of visceral dissemination be a correct one, it should be possible to show:—

(*a*) That the abdomen may be invaded independently of the thorax and *vice versâ*.

And both for the peritoneal and pleural cavities it has to be proved:—

(*b*) That its subserous lymphatic plexus is connected by fine anastomoses with the fascial plexus which lies beneath the subcutaneous fat.

(*c*) That along these connecting vessels permeation extends from the fascial to the subserous plexus.

(*d*) That in consequence cancer cells escape into the serous cavity.

(*e*) That these cancer cells are capable of becoming re-implanted at various points on the serous membrane, and so of giving rise to metastases.

(*f*) That if the serous cavity is obliterated by adhesions, and trans-cœlomic implantation is thus prevented, dissemination is delayed.

(*g*) That the distribution of the visceral metastases is such as would be expected from this mode of origin, and more especially that they primarily affect the surface of the viscera, and that owing to the action of gravity they are found most abundantly at the lower limits of the serous cavities.

Abdominal and Thoracic Invasion often Independent Events.

Thoracic metastases occur without any invasion of the abdomen in 10 per cent. of early, and in 22 per cent. of late cases (see next chapter). Conversely, abdominal metastases occur without any invasion of the thorax in 17 per cent. of the early and in 11 per cent. of the late cases. The latter fact especially is a very striking one, to which attention cannot be too strongly directed. For according to accepted theories the cancerous emboli which infect the abdomen must always have passed through the thorax by way of the pulmonary vessels. On such an hypothesis abdominal invasion should always be secondary to thoracic invasion, whereas it would appear from the figures I have quoted that, in point of fact, invasion of the abdomen and invasion of the chest are, or may be, entirely distinct events, requiring separate consideration. Invasion of the abdomen will be considered first.

Epigastric Invasion of the Abdomen through its Parietes.*

In the Autumn of 1903, I was present at the autopsy on a case of breast cancer, of which the following is a brief account:—

Epigastric Invasion, Case I.—Ann F., aet. 63. Twenty-one months before death the left breast and axillary glands were removed for cancer. Two months before death she was readmitted with numerous subcutaneous nodules in the region of the scar, especially below it, where they extended nearly to the costal margin. Three weeks after readmission a large mass diagnosed as omental growth was felt in the abdomen.

At the autopsy no glandular or other metastases were found in the thorax, while in the abdomen they were numerous. The left lobe of the liver was riddled by secondary deposits, which in the right lobe were more sparsely distributed. The fat around the pylorus contained numerous cancer nodules. An irregular nodular line of growth ran along the mesenteric attachment of the small intestine. Douglas's pouch was filled by a mass of diffuse growth, in which the ovaries lay embedded. The omentum appeared normal, though one or two cancerous glands were present in it high up. The large abdominal

* A fuller account of this subject is contained in my Astley-Cooper Prize Essay, 1904, at present unpublished.

mass which made its appearance just before death proved to be a diffuse cancerous infiltration of the mesentery, apparently spreading from the lumbar glands. None of the retro-peritoneal organs were invaded by cancer.

In this case it seemed quite certain that cancer cells had escaped into the peritoneal cavity, and had implanted themselves at various points. Only the organs covered by peritoneum were cancerous. The filling of Douglas's pouch by a diffuse mass of growth, matting the pelvic structures, a condition which is recorded four times in 422 autopsies, showed the influence of gravity on the site of implantation. The condition of the omentum, which appeared normal to the naked eye, was especially interesting, and it will be convenient to consider here certain points in connection with omental secondary growths.

Omental Cancer.

Cancer of the omentum occurred in only 1 per cent. of the cases of breast cancer which I have collected, and this is an obvious argument against the view that escape of cancer cells into the peritoneal cavity is a frequent event. But a microscopic section of the apparently normal omentum in Case 1 showed it bordered by a false membrane containing degenerate cancer cells (see Fig. 30). The omentum does not escape implantation of cancer cells upon its surface, but its pre-eminent encysting power usually, though not invariably, enables it to protect itself against invasion.

The most interesting form of omental cancer is that in which numerous secondary growths hang from its surface as cancerous polypi, attached by delicate non-cancerous pedicles. Specimen 1227, Guy's Hospital Museum, is an excellent instance of this condition. In such cases trans-cœlomic implantation is seen in its most unequivocal form.

Beneke is stated by Borst to have observed in peritoneal fluid minute spherules of cancer cells surrounded by an organized layer of non-vascular lymph. Often, no doubt, the cancer cells thus encysted are destroyed, but sometimes pedunculated omental secondary growths result, owing to the adhesion of these encysted masses to the great omentum, and to their continued growth. In a later stage the polypoid

growths become sessile, and invade the substance of the omentum, which is at last seen as a transverse tumour puckered up along the lower border of the transverse colon.

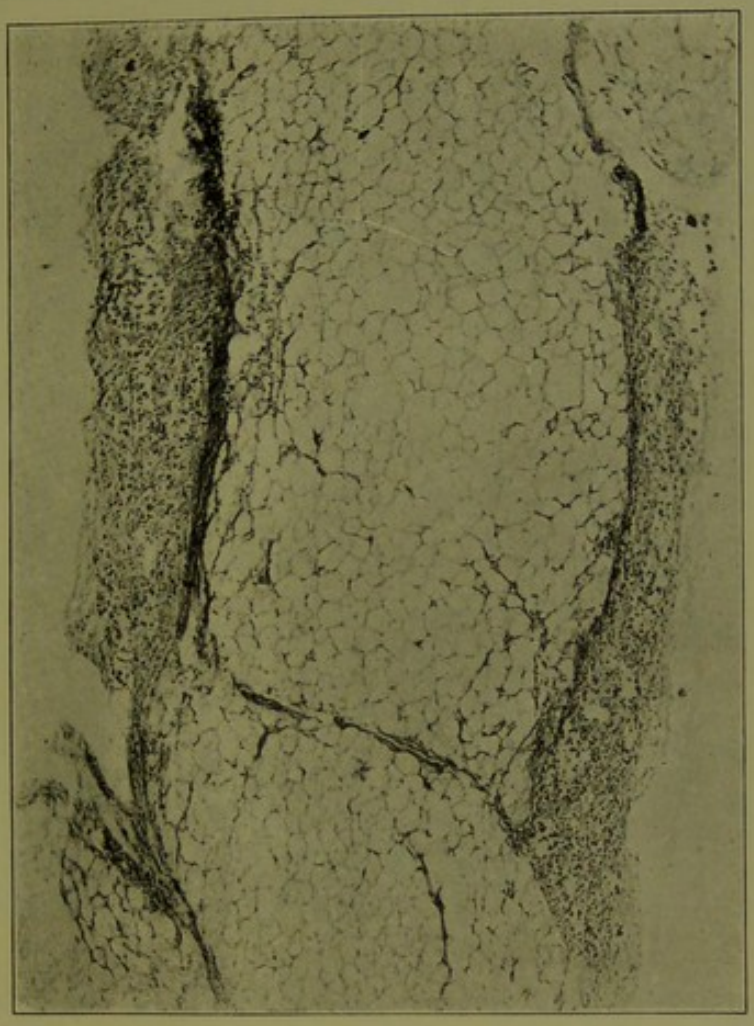


FIG. 30.

Case of Ann T. Vertical section of omentum near its free edge. The omentum, which appeared normal to the naked eye, is bordered by a false membrane in whose meshes are seen encysted cancer cells. They appear somewhat degenerate, but are nevertheless invading the substance of the omentum here and there.

This section, apart from any other evidence, gives conclusive proof of the occurrence of transperitoneal implantation.

But to return to Case I., the main problem it presents may be stated as follows:—In the absence of invasion of the thorax, how did cancer obtain access to the abdomen?

The presence of subcutaneous nodules nearly as far down as the left costal margin, and the predominant incidence of cancer upon the left lobe of the liver, suggested a direct invasion of the abdominal cavity through the epigastric parietes, where the liver lies in contact with them.

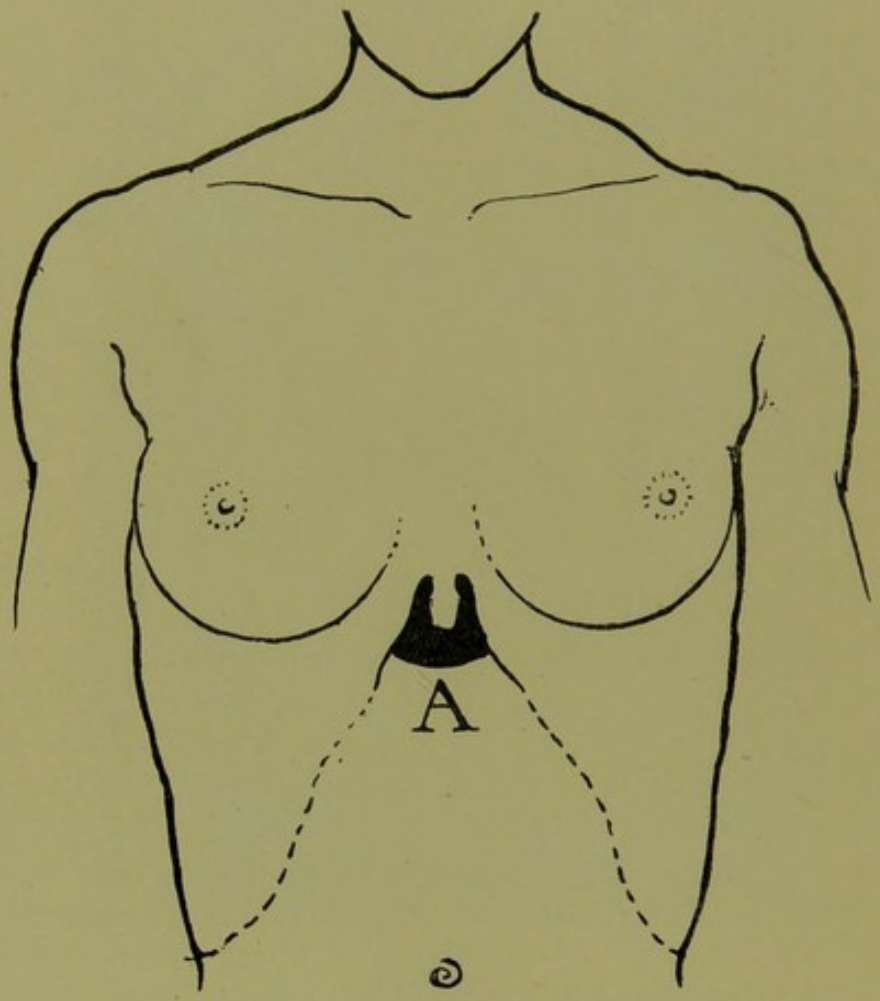


FIG. 31.

The area (A) of epigastric invasion in breast cancer. Its lower limit is a purely artificial line. This area might not inappropriately be called the dangerous area in breast cancer.

An opportunity of testing this hypothesis presented itself in the next two cases. Though in both these cases the chest as well as the abdomen was invaded, the *direct* evidence of invasion through or near the area represented in Fig. 31, was conclusive.

Epigastric Invasion, Case II.—Emily C., aet. 36 Two years before death the right breast was removed for carcinoma. At the autopsy the thoracic wall showed an extensive cancerous ulcer, extending inwards to the middle line, and outwards to the axilla. The ulcer had invaded the underlying muscles and pleura. The left pleura and

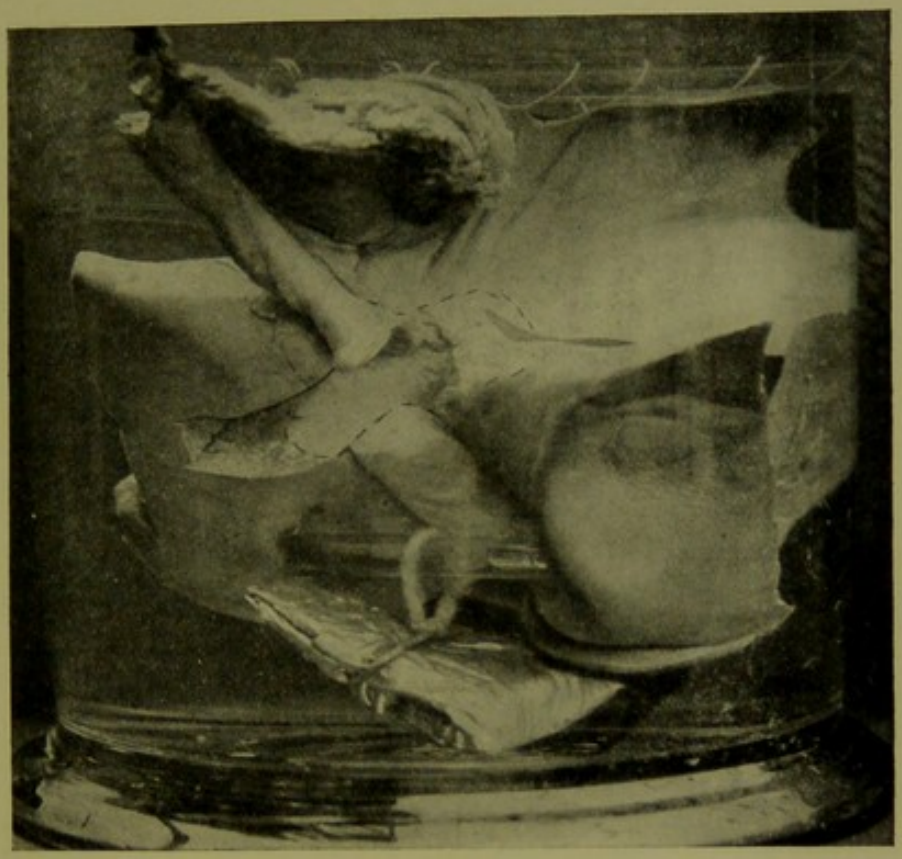


Fig. 32

The round ligament is seen passing into the umbilical notch between the right and left lobes of the liver. The lateral and posterior portions of the liver have been cut away. Above the round ligament is seen the pad of fat which intervenes between the two layers of the falciform ligament along the line of its attachment to the anterior abdominal wall. As a result of epigastric invasion, a large solitary cancer nodule (surrounded by a dotted line) occupies the anterior edge of the liver at the umbilical notch. The rest of the liver was healthy.

pericardium also showed cancer. The axillary, supra-clavicular, and posterior mediastinal glands were cancerous.

The only visceral metastases were a large solitary nodule in the liver at the umbilical notch (see Fig. 32), and nodules in both ovaries.

In the vicinity of the primary growth were some scattered subcutaneous nodules. The lowest of these was situated eight inches above the umbilicus. It was found that permeation of the deep fascia had extended downwards two and a half inches below this nodule (see

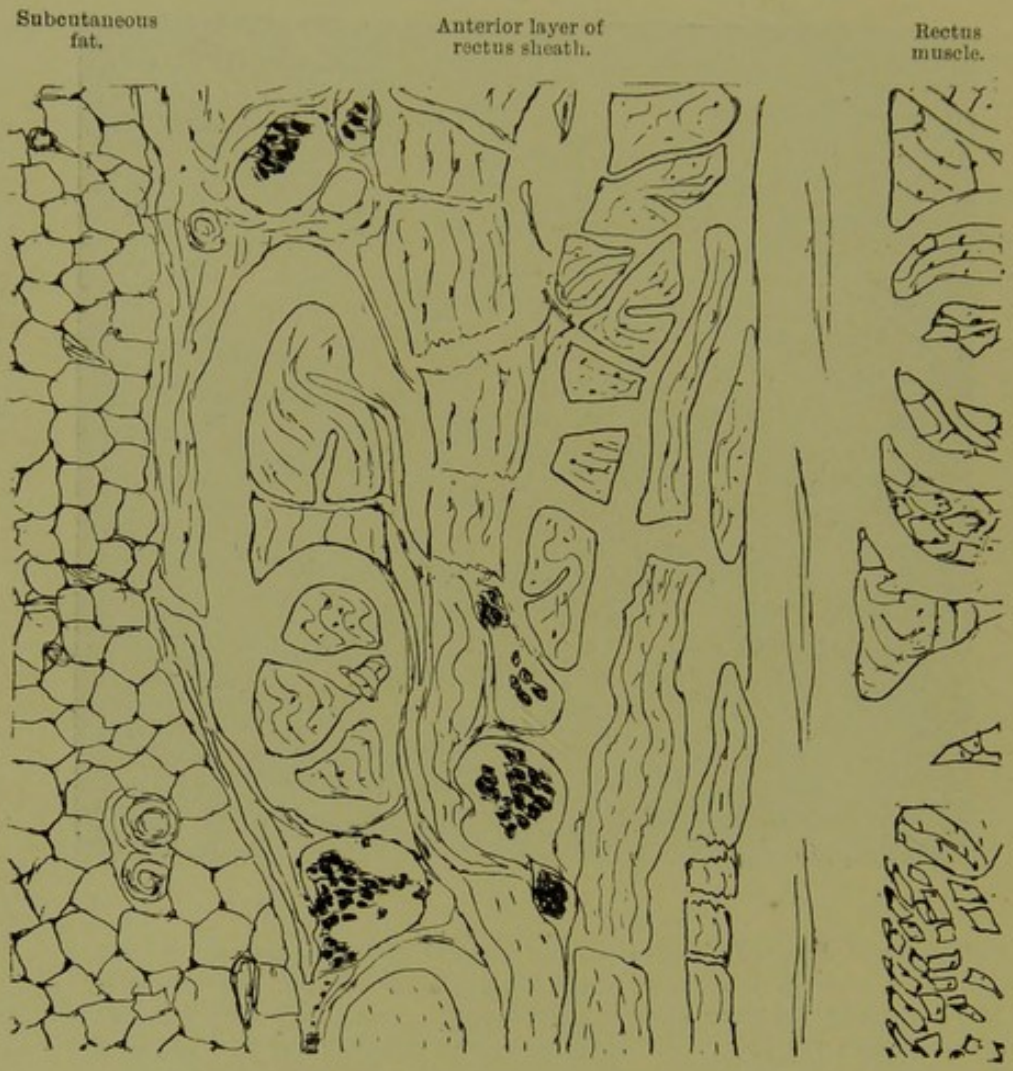


FIG. 33.

From Case II. of epigastric invasion. Permeated lymphatics blocked by cancer cells upon the anterior layer of the rectus sheath 5½ inches above the umbilicus.

Fig. 33). Higher up minute cancer nodules were found upon the anterior layer of the rectus sheath (see Fig. 34). At the level of the tip of the ensiform cartilage the rectus muscle was deeply invaded by growth, and here a fibrous septum containing permeated lymphatics was traced

3 mm. backwards into the substance of the muscle (see Figs. 35, 36, 37, and 38). In order to trace the further course of the growth, sections of the falciform ligament and of the included round ligament of the liver were made at different points. (*a*) In a section of the falciform ligament about three inches long, parallel to, and 6 mm. distant from, the convex surface of the liver, growth was found about

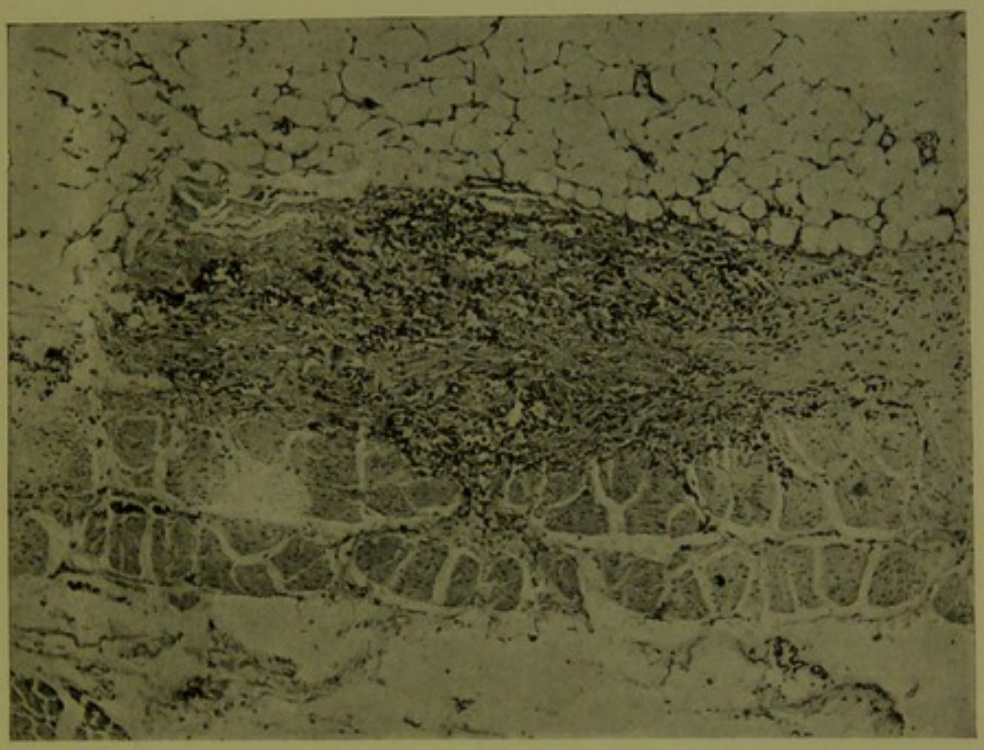


FIG. 34.

From Case II. of epigastric invasion. A microscopic cancer nodule lying upon the anterior layer of the rectus sheath in the epigastric region. Lines of cancer cells are seen passing between the fibrous bundles of the rectus sheath to invade the interior of the rectus sheath. A minute portion of the anterior surface of the rectus muscle is visible in the extreme left lower corner of the figure.

3 mm. from the anterior margin of the ligament. (*b*) In a section near the umbilicus where the parietes had been proved free from growth none was found in the round or falciform ligaments. (*c*) In a section of the round ligament just behind the umbilical notch, scattered cancer cells could be seen in the sub-endothelial tissue all round it. (*d*) A section of the falciform ligament near its posterior limit was free from growth.

FIG. 35.

From Case II. of epigastric invasion. A horizontal section through the rectus muscle and the anterior layer of its sheath in the epigastric region of the abdomen. B B is the anterior layer of the rectus sheath; D, the deepest portion of a cancer nodule which lay upon it; C C is a fibrous septum running horizontally backwards into the substance of the rectus muscle. Along its whole length it shows permeated lymphatics and interstitial cancerous infiltration. A solitary nodule of cancer was present in the liver at the umbilical notch.

In this case it was shown (1) that fascial permeation had extended considerably below the ensiform cartilage, (2) that the rectus muscle in the epigastric angle was in consequence deeply invaded by cancer, (3) that at the same level there

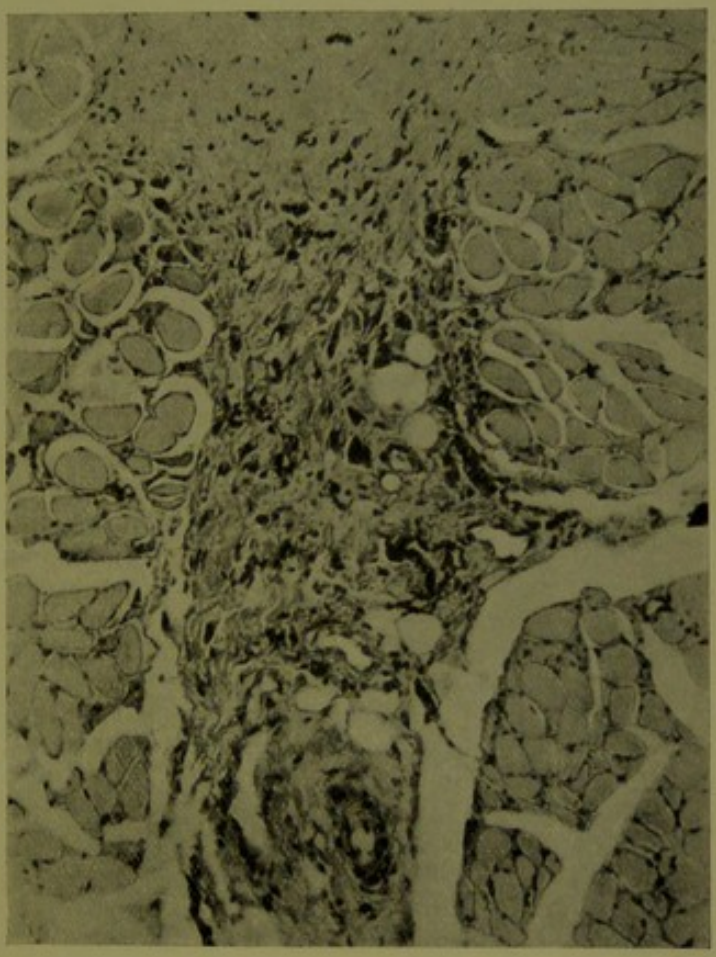


FIG. 36.

From Case II. of epigastric invasion. A photograph showing, more highly magnified, a portion of the fibrous septum of the rectus muscle represented in Fig. 35. It is infiltrated by irregular lines of darkly-stained cancer cells.

was a large solitary nodule in the contiguous portion of the liver. The escape of cancer cells into the cœlom, their gravitation into the pelvis, and their subsequent implantation, were shown by the nodules in each ovary—the only other abdominal metastases.

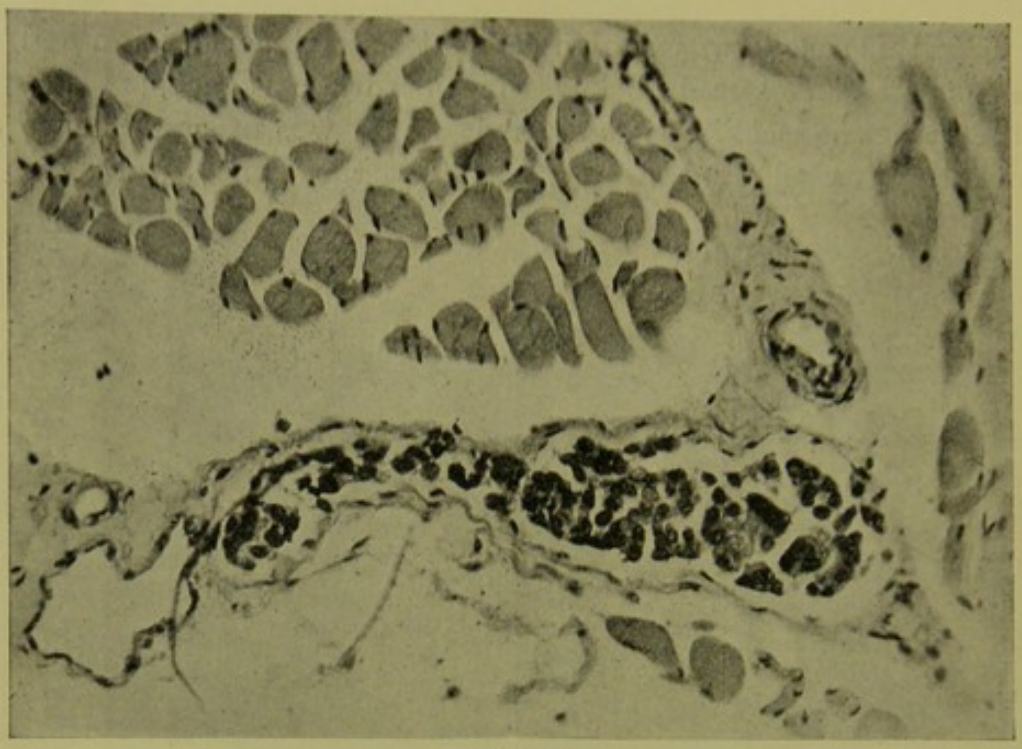


FIG. 37.

From Case II. of epigastric invasion. A highly magnified longitudinally cut lymphatic, full of darkly stained cancer cells, lying in the rectus muscle at the level of the tip of the ensiform cartilage. Near the permeated lymphatic are seen small normal blood-vessels.

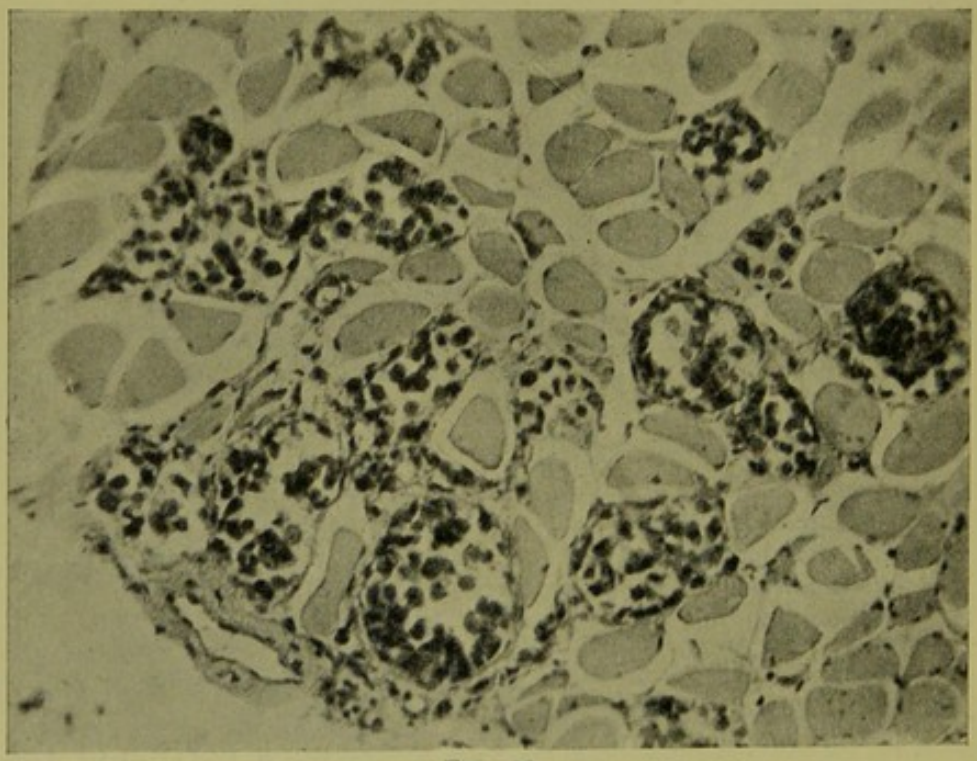


FIG. 38.

From Case II. of epigastric invasion. A section of the rectus muscle near the level of the tip of the ensiform cartilage, showing various stages in the invasion of the muscle-fibres which follows permeation of the intra-muscular lymphatics. The cancer cells proliferate within the interior of the muscle fibre, replacing its substance and distending the sarcolemma.

It will be noted that in this case epigastric invasion was apparently subsequent to, though not consequent on, invasion of the thorax. If this were usually the case the surgical interest of epigastric invasion would be comparatively slight.

Epigastric Invasion, Case III.—Constance C., aet. 57, died of cancer of the left breast two years after it was first noticed. Ten months before death she became jaundiced, and at this time the left breast was

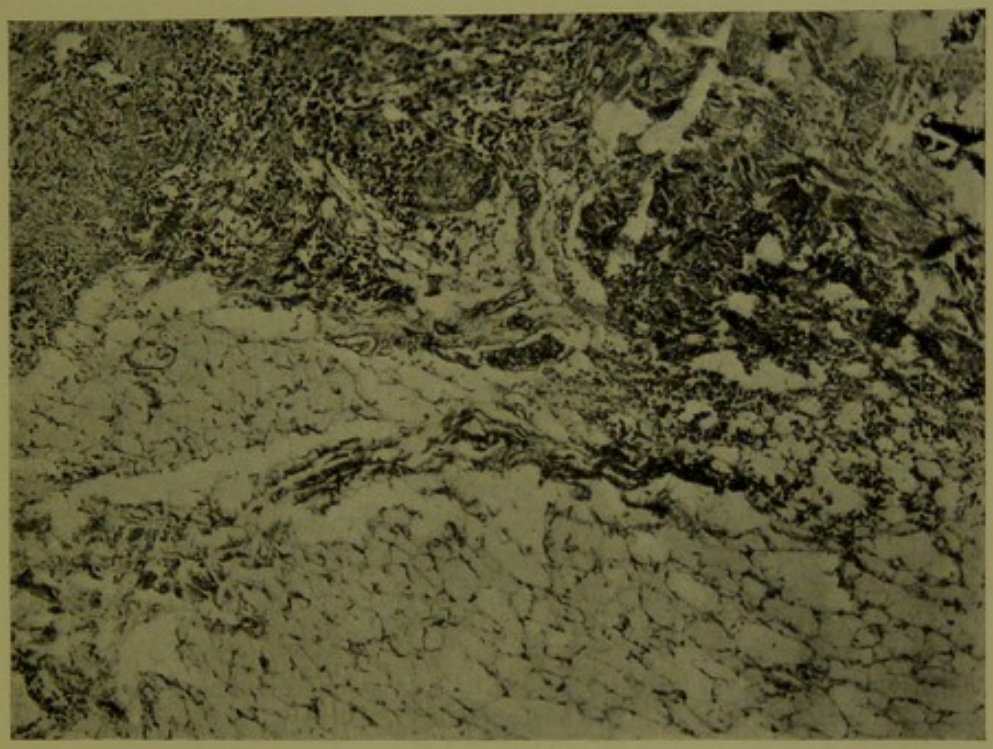


Fig. 39.

From Case III. of epigastric invasion. A section through the linea alba and the sub-peritoneal fat just below the tip of the ensiform cartilage. The line of junction of these two layers forms the equator of the figure. Lines and groups of cancer cells are seen filling the interspaces between the fibrous bundles of the linea alba, and debouching thence upon the sub-peritoneal fat.

represented by a shrunken ulcerated scirrhus puckering the surrounding skin. The reporter notes that there was marked tenderness just below the ensiform cartilage, but no obvious enlargement of the liver. A hard lump appeared in the *right* breast just before death. At the autopsy there was cancer *en cuirasse* over the left side of the chest. At the time of death the ulceration of the primary growth had healed. The growth had extended through the chest wall, the pleura and pericardium

beneath showed minute nodules, and some of the bronchial glands were cancerous. There were no other deposits in the chest. No operation had been performed.

Upon the convex surface of the liver, in the neighbourhood of the falciform ligament a few small nodules of cancer were visible, but none were present in the substance of the organ. Near its outlet, the common bile-duct was surrounded and constricted by a nodule of growth. The left kidney showed cancer at one point on its surface. On the pelvic peritoneum were some small flat nodules.

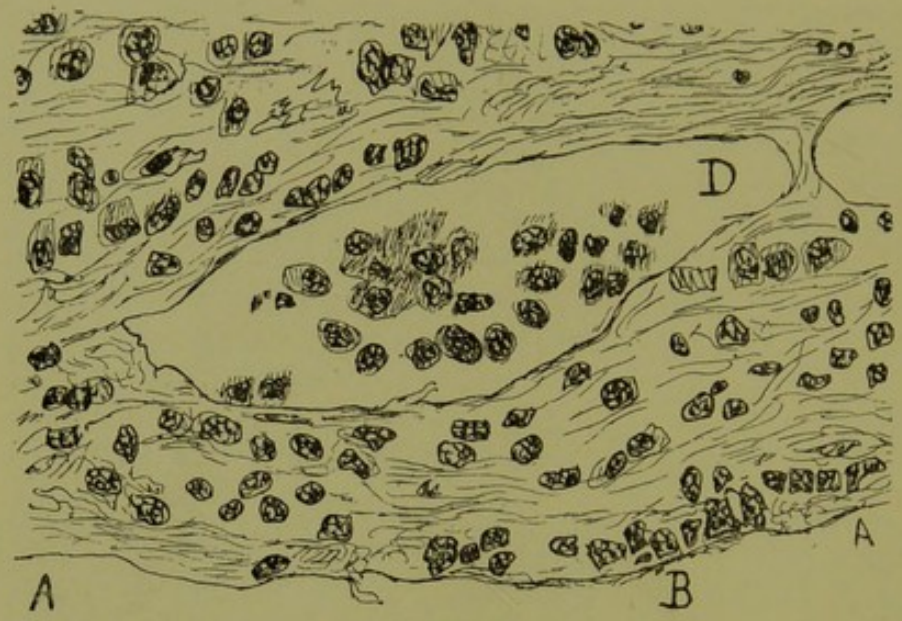


FIG. 40.

A portion of the epigastric parietal peritoneum at a point opposite to the preceding figure. D is a permeated vessel of the subserous lymphatic plexus. The sub-endothelial tissues are crowded with cancer cells, which at B are evidently escaping into the peritoneal cavity.

On the parietal peritoneum at the level of the tip of the ensiform cartilage a few miliary nodules were visible. Above and below this point the peritoneum appeared normal. This was especially noted to be the case at the attachment of the diaphragm to the ensiform cartilage. A vertical section of the entire thickness of the abdominal wall from skin to peritoneum in the sub-xiphoid region showed the following points: (*a*) The skin was free from growth, (*b*) the deeper part of the subcutaneous fat was extensively infiltrated, while the more superficial layers were comparatively free, (*c*) the deep fascia was much thickened and infiltrated throughout by growth, (*d*) the fibrous bundles of the linea alba on its superficial surface were much eroded by growth. Lines of cancer cells could be seen passing between its bundles, and debouching

on the sub-peritoneal fat (see Figs. 39 and 41). The transversalis fascia is in this situation hardly recognisable as a distinct layer. (*e*) The sub-peritoneal fat, between whose bundles wide empty interspaces were seen, was practically free from growth. Though it had itself escaped, it could offer but a minimum of resistance to the passage of

FIG. 41.

From Case III. of epigastric invasion. A highly magnified portion of Fig. 39. Numerous cancer cells are seen lying between the fibrous bundles of the linea alba, and debouching thence upon the sub-peritoneal fat, which is seen in the lower part of the figure.

cancer cells through it. (*f*) The peritoneum showed cancerous permeation of the sub-endothelial lymphatic plexus (see Fig. 40); many cancer cells were also lying in the cellular interspaces. In places the peritoneal endothelium overlying the cancer cells was degenerate. Quite evidently at these points cancer cells were entering the peritoneal cavity.

In each of three sections taken at different levels through the falciform and round ligaments between the umbilical notch and the anterior abdominal wall, a small area of cancerous permeation was found in the falciform ligament. The permeated lymphatics were found only in the *left* layer of the fold of peritoneum, the layer to which (owing to the attachment of the falciform ligament to the posterior layer of the right rectus sheath an inch to the right of the middle line) cancer would first naturally extend from the epigastric peritoneum. The two laminae of the ligament are here separated by a thick pad of fat. If growth had extended downwards through the diaphragm, one would naturally expect the impartial invasion of *both* laminae. Moreover, a section of the falciform ligament far back under the diaphragm was found to be free from growth.

The escape of cancer cells into the peritoneum was shown in this case merely by a few small nodules on the convex surface of the liver. Gravity had carried a few cells into the pelvis, where they had given rise to small peritoneal nodules.

The permeated lymphatics found in the falciform ligament are anatomically known to lead to or from the portal glands. Accordingly a group of metastases, doubtless due to centrifugal permeation round the invaded glands, was found in their immediate vicinity. Permeation from these glands appears to have given rise to the pyloric nodule and to that in the bile duct. The only remaining abdominal focus was that in the right kidney (see later, Retro-peritoneal Invasion).

It appears then that of three autopsies, all occurring within the space of three months, presumptive evidence of epigastric invasion was obtained in the first one, and conclusive evidence in the last two. During this period an average total of five autopsies on breast cancer might be expected at the two hospitals concerned. The inference that epigastric invasion is a frequent event seems unassailable.

Anatomy of the Epigastric Angle.

It is somewhat remarkable that, so far as I can find, it has never been suggested, even as an armchair hypothesis, that breast-cancer directly invades the abdomen through the epigastric parietes. Mr. Sheild, for instance, says:—"It seems hardly logical to assume that cancer(s) of the ovary, uterus, or liver, occurring perhaps years after an amputation of the mamma, are true recurrences in the strict sense of the word. Their occurrence, however, is very mysterious and significant,

and at present wrapped in obscurity." And yet the anatomy of the epigastric region strongly suggests the likelihood of the mode of invasion which I have just described. According to the researches of Stiles the lower and inner margin of the breast overlies the sixth costal cartilage. That is to say, this part of the mammary circumference is distant only about an inch from the interspace between the ensiform and the seventh costal cartilages. Hence, as soon as parietal permeation has extended little more than an inch beyond the edge of the breast, the cancerous lymphatics of the deep fascia are no longer separated from the subserous (subperitoneal or subpleural) fat by a bony cage of many layers covered by thick muscles, but simply by a single layer of fibrous tissue, traversed by lymphatics. For at the tip of the ensiform cartilage the transversalis fascia is hardly recognisable as a distinct layer, and the parietal lymphatic plexus is separated from the subperitoneal fat simply by the linea alba. It is not surprising if, through this obviously weak spot, cancer frequently reaches the peritoneum before it has succeeded in reaching the pleura, even at points directly subjacent to the primary focus.

CHAPTER VI.

VISCERAL DISSEMINATION (continued): A STATISTICAL STUDY OF EPIGASTRIC INVASION OF THE ABDOMEN.

THE occurrence of epigastric invasion has now been histologically proved in two cases. It is impossible single-handed to examine a large number of cases by this laborious method. To obtain a broad view of the subject it is necessary to turn to post-mortem records.

Statistical Data of Early and of Late Cases.

It will frequently be necessary to refer to the data which I have obtained from the pathological records of the Middlesex and of Guy's Hospitals for the thirty years, 1871—1900. The two records have been kept separate for the purpose of comparison since they are entirely different in character. Owing to the right of patients in the special cancer wards of the Middlesex Hospital to remain until "relieved by art or released by death," a large proportion of the necropsies are on cases which have run their full course. Guy's Hospital possesses no special cancer wards, and the pressure on its accommodation leaves no room for this class of case in the surgical wards. Hence in the smaller total of necropsies at Guy's Hospital there is a large proportion of cases still in the operable stage—of cases which died after operation, or from intercurrent disease. No less than 49 per cent. of the ninety-three cases from Guy's Hospital come under this heading, as opposed to 9 per cent. of the 329 Middlesex Hospital cases. Naturally a large majority of the post-operative fatalities occurred in the earlier (pre-antiseptic) portion of the period under review, while the number of necropsies at the Middlesex Hospital has remained practically constant, for the reasons specified.

These two sets of cases will be referred to as the "early" (Guy's Hospital), and the "late" (the Middlesex Hospital) set of cases, though of course some late cases occur in the Guy's Hospital records, and some early ones in those of the Middlesex Hospital. It will later appear that the marked difference in character between these two series of cases allows certain important conclusions to be drawn.

The Early Stages of Abdominal Invasion.

Cases in which abdominal growth is present only in a single organ or pair of organs are to be regarded, not as examples of the haphazard incidence of cancer, but as indicating the usual starting points of the attack on the abdominal viscera. When only one organ is affected, it may be inferred that the invasion is in an early stage, unless, as is often the case in the liver, the organ is extensively infiltrated. Of the whole number of cases a single abdominal organ, or pair of organs, was affected in 115, i.e. in 27 per cent. The annexed table shows the incidence upon the various organs.

TABLE III.

Derived from 422 cases of Breast Cancer, showing in what number of instances, either with or without other metastases, a single *abdominal* organ or pair of organs, was affected by cancer.

		Guy's Cases.	Middlesex Cases.	Total.
Viscera Covered by Peritoneum	Liver	13	77	90
	Portal glands ...	1	1	2
	Ovaries	1	2	3
	Uterus	0	1	1
	Pelvic Peritoneum ...	0	1	1
	Peritoneum	0	4	4
	Mesentery	1	1	2
	Intestine	1	0	1
	Spleen	0	1	1
Retro-Peritoneal Viscera	Right kidney ...	0	4	4
	Left kidney... ...	0	1	1
	Both kidneys ...	0	1	1
	Right adrenal ...	0	1 (?)	1 (?)
	Lumbar gland ...	0	1	1
	Lumbar vertebra ...	0	2	2
		17	98	115
		Out of 93 cases = 18 %	Out of 329 cases = 29 %	Out of 422 cases = 27 %

An account of abdominal dissemination must explain, not only why the liver is usually the point of first attack, but also why the pelvic viscera, and to a less extent the portal glands and the peritoneum, may exceptionally meet the first onset of the growth. The ten cases in which cancer was invading the abdomen retro-peritoneally also require explanation. This is evidently a later event than trans-peritoneal implantation, for it occurs only in the later series of cases (see p. 135).

Analysis of the Cases into Groups.

In the absence of direct evidence for any other hypothesis it is legitimate to assume epigastric invasion in all cases where the thorax has escaped invasion, and where at the same time metastases are present in the viscera intimately related to the peritoneum.

There were seventy cases, out of a total of 422, which showed abdominal metastases, but no thoracic ones.

On looking through these seventy cases it became evident that they did not form a homogeneous collection, but grouped themselves in the following sub-divisions :—

(*a*) Cases, fifty-three in number, in which those abdominal viscera are cancerous, which come into intimate relation with the greater sac of the peritoneum. The viscera most frequently affected are the liver and the pelvic organs.

(*b*) Cases in which the metastases occur in the retro-peritoneal organs, that is to say, in the suprarenal bodies, the kidneys, the lumbar glands, the pancreas, and the posterior portion of the liver. These cases, seven in number, occur exclusively in the late series, and are considered later under the heading, "Retro-peritoneal Invasion."

(*c*) Cases in which the abdominal infection is possibly complicated by a blood infection. This group consists of six cases, in five of which the abdominal infection is trans-peritoneal, while in one it is retro-peritoneal.

It is most likely that in these cases, which are, M. 241, 79, M. 118, 87,* M. 57, 88, M. 6, 01, G. 375, 76, and G. 273, 99, the blood infection was a late event, and had no share in producing the abdominal metastases, which preceded the blood infection and occurred by the ordinary channels. But in order to prevent the introduction of a source of fallacy they have been excluded from classes A and B. No further reference need be made to them.

(*d*) Cases in which both the organs covered by peritoneum and the retro-peritoneal organs are affected.

This class contains four cases, which are:—

M. 178, 73, Metastases in liver, and the right kidney.

M. 175, 83, Metastases in liver and kidneys.

M. 175, 98, Metastases in liver, left suprarenal, and retro-peritoneal glands.

G. 465, 75, Metastases in liver (nodules chiefly superficial) both suprarenals, left kidney.

In these cases both series of organs may have been infected primarily, or either secondarily to the other. No deductions can therefore be drawn from them.

Subtracting the other three classes we have left for consideration the fifty-three cases forming Class A, in which while the thorax is free from growth, those abdominal organs which are in close relation to the peritoneum show metastatic deposits.

In all these cases there is evidence either (*a*) of the implantation upon the visceral serous surfaces of cancer cells which have escaped into the peritoneal cavity, or (*b*) of infection of the liver along the lymphatic tract which runs from the falciform ligament to the portal glands. Either of these events might occur from the penetration of the diaphragm by intra-thoracic growth. But in all these cases invasion of the abdomen through the diaphragm (diaphrenic invasion) is excluded by the freedom of the chest from growth. I shall

* M. 118, 87, is an abbreviation for Autopsy No. 118, The Middlesex Hospital, 1887. Cases from Guy's Hospital are similarly indicated by the letter G.

be able to show that diaphrenic infection only occurs with difficulty, and in a very late stage of thoracic infection (see p. 137). All the evidence goes to show that it does not occur in the early invisible stage of thoracic infection which may have been present in some of these 53 cases.

In several of the cases the abdominal infection had reached a very advanced stage :—

G. 379, 75.—Cancer of the left breast. No operation. Deposits in left axillary and cervical glands. Lumbar glands extensively cancerous. Mesentery studded with small deposits. A large mass in the neighbourhood of the left ovary invading the Fallopian tube. The ovary was the size of a foetal head. Douglas's pouch was partly obliterated by growth, and there were nodules on the pelvic peritoneum. The portal glands were slightly enlarged. The chest was quite healthy.

G. 253, 91.—Scirrhus of left breast. Mass of growth surrounding, but not involving, the uterus and the wall of rectum. Numerous flat plaques of growth over the peritoneum. Aortic glands cancerous. A mass of growth extends along the round ligament for some distance into the liver. No secondary growth in the thorax.

In such cases as these it is in the last degree improbable, if the abdomen had become infected from the thorax, that the abdominal secondary deposits could have reached such an advanced stage while the thoracic growths still remained invisible to the naked eye.

By a process of exclusion, starting with 422 cases, we have then obtained a residuum of 53 cases in which cancerous infiltration of the epigastric parietes seems the only likely explanation of the metastases found in the abdomen. That is to say, pure epigastric invasion apart from infection of the thorax, or by way of the blood, is found at the time of death in 12 per cent of all cases of breast cancer.

It must be emphatically stated that this percentage by no means represents the total number of cases in which epigastric invasion occurs. It must often happen, after the thin epigastric parietes have been pierced, that the patient survives until the growth infiltrates also the thicker thoracic wall and so invades the thoracic cavity. More rarely thoracic invasion may occur while the abdomen remains intact, and yet by the time death takes place epigastric invasion may independently supervene. All such cases—cases in which the necropsy

reveals metastases both in the abdominal and the thoracic cavities—are at present excluded from consideration.

It is very important, if possible, to determine whether as a general rule epigastric infection occurs before the primary growth has infiltrated the chest wall, or whether such an event is the exception.

It has been shown that the cases from Guy's Hospital are chiefly early ones, few in number, and representing the percentage mortality of a very large number of operations; while those from the Middlesex Hospital are mostly late ones. It will, therefore, be interesting, as showing whether epigastric infection is an early or a late event, to find out in which of these two sets of cases it is most frequently met with in an unmixed form.

Among the fifty-three cases of pure epigastric invasion, thirty-seven occurred in the Middlesex series out of 329 cases, and sixteen in the Guy's series, out of 93 cases. Working out these figures as percentages it appears that among 100 patients who die early in the course of cancer of the breast, unmixed epigastric invasion is found in seventeen cases, at a time when only ten cases show intra-thoracic growth, while among those who die late in the disease epigastric infection is found alone only in eleven cases out of 100.

TABLE IV.

Showing the infection percentages of the thorax and abdomen in an early (Guy's Hospital) and a late (the Middlesex Hospital) set of cases.

	Guy's Hospital (early cases).	The Middlesex Hospital (late cases).
Metastases present in abdomen and not in thorax (Abdominal Group)...	17 per cent.	11 per cent.
Growth in thorax and not in abdomen (Thoracic Group)	10 „	22 „
Metastases present in both thorax and abdomen (Abdomino-thoracic Group)	20 „	35 „
No metastases present (except in axillary glands)...	40 „	23 „
Other cases (e.g. bone infection)	13 „	9 „

This table demonstrates that early cases show, as might be expected, a larger percentage of the "no metastases" cases, and a smaller percentage of cases with thoracic metastases, or with both thoracic and abdominal metastases.

On the other hand there is this apparently anomalous fact, that the early series shows, as compared with the late series, a considerably larger percentage of cases in which the abdomen is affected by cancer, while the thorax has escaped. This, of course, implies subsequent invasion of the chest in a certain number of cases in which at first the abdomen alone was infected. Such cases then pass into the "abdomino-thoracic" group. No other explanation of the diminution is possible. Assuming, therefore, that the two sets of cases only differ in their time relations, that the Guy's cases, if they had lived long enough, would have assimilated themselves statistically to the Middlesex cases, there is no escape from the conclusion that in certain of the "abdomino-thoracic" group thoracic infection occurred subsequent to abdominal infection, and that the primary visceral invasion in these cases took place through the epigastric parietes.

It is clear then that epigastric infection of the abdomen frequently precedes invasion of the thorax. It, therefore, possesses a surgical importance even greater than would be suggested by the fifty-three cases where, at the time of death, it was still present in an uncomplicated form.

All the cases in which epigastric invasion can possibly have occurred are included in the abdominal and abdomino-thoracic groups. Adding them together, we find that in the early set of cases the highest possible frequency of epigastric invasion was 37 per cent., and in the late set 46 per cent.

From the smallness of the difference between these maximal figures it may be concluded, though not with certainty, that if epigastric infection does not occur in the early stage of breast-cancer the chances of its supervening later are not very great. This conclusion is borne out by the marked increase of the thoracic group of cases in the later series, an increase which would otherwise show itself in the abdomino-thoracic group.

From these facts I should be inclined to argue that the occurrence or non-occurrence of epigastric infection depends, not only on the point of origin of the primary growth in the breast, but, to some extent, on variations in the freedom of communication between the hepatic and parietal lymphatics

in the epigastric angle. The inconstancy of the lymphatic nodules sometimes found in this region proves that such variations exist.

The increase in the thoracic group in the latter series shows that infection of the thorax, though later in beginning, is more certain ultimately to make its appearance.

It is impossible, statistically, to fix the total percentage of cases in which epigastric infection occurs, whether in a mixed form or alone. The minimum limit is fixed by the number of cases in which epigastric infection occurs alone, i.e. 12 per cent., the maximum by adding this number to that percentage of cases in which both the thorax and the abdomen show metastases, i.e. 32 per cent., on the whole number of cases from Guy's and the Middlesex Hospitals. The percentage of cases in which epigastric invasion, whether pure or mixed, occurs is thus between 12 per cent. and 44 per cent. In my opinion the latter figure is nearer the truth than the former.

The Abdominal Deposits in Fifty-three Cases of Pure Epigastric Invasion.

Since many of the cases in this group must be early ones, it is not surprising that in forty of them metastases were present only in one abdominal organ or pair of organs. Such cases are presumably in an early stage, and are important as indicating at what point of the abdomen invasion occurs. The liver was invaded in 36 cases, both ovaries in two cases, the capsule of the spleen in one case, the edge of the mesentery in one case. Owing to its close contact with the cancerous epigastric peritoneum, and to its lymphatic relations with the portal glands, the liver is nearly always the first organ to suffer. Rarely cancer-cells may fall through the peritoneal cavity and cause pelvic metastases before the liver is invaded.

In five cases out of 53 there are abdominal metastases in two abdominal organs.

These cases are :—

M. 16, 76. Cancer of left breast. Metastases in liver and right ovary.

M. 195, 77. Cancer of right breast. Metastases in peritoneum, intestines matted by growth.

M. 141, 83. Cancer of left breast. Metastases in liver and retro-peritoneal glands.

M. 31, 00. Cancer of left breast. Metastases in liver and fifth lumbar vertebra.

G. 4, 81. Cancer of left breast. Metastases round neck of gall-bladder and in one portal gland.

In the remaining eight cases the metastatic deposits were multiple.

TABLE V.

Cases of Breast Cancer showing Epigastric Invasion with multiple abdominal Metastases.

Reference No. of Case.	Side of Primary Growth.	Situation of Metastases.
M. 50, 78 ...	Left.	Nodules upon intestines. Mass of growth round abdominal aorta and inferior vena cava.
M. 37, 87 ...	Left.	Liver, spleen, ovaries.
M. 66, 91 ...	Left.	Two nodules in liver, pelvic peritoneum, peritoneum over fundus uteri.
M. 28, 01 ...	Right.	Liver (almost replaced by growth). Gall-bladder. Portal and aortic glands.
G. 130, 74 ...	Right.	Portal glands. Several nodules in liver. Two in gastric mucosa, cardiac end.
G. 49, 75 ...	Right.	Liver crowded with nodules, weight 128 ozs. Gall-bladder. Portal and aortic glands. Right ovary and surrounding fat.
G. 379, 75...	Left.	Portal glands (slightly). Mesentery, left ovary (size of fœtal head) and Fallopian tube. Pelvic peritoneum. Lumbar glands (extensively).
G. 253, 91 ...	Left.	Growth extending into liver along round ligament, but no other metastases in it. Mass of pelvic growth. Universal plaques over peritoneum. Nodule in common bile duct.

The following table shows the various metastases which may be present in cases of pure epigastric invasion, and their predominant incidence upon the liver and the pelvic organs.

TABLE VI.

Showing the frequency of invasion of the various abdominal organs in fifty-three cases of uncomplicated Epigastric Invasion.

Organ affected.	Probable mode in which the infection arises.	In what Number of Cases.	Percentage of Total.
Liver	By contact with cancerous epigastric peritoneum, or by secondary invasion from portal glands ...	45	84
Portal glands ...	Invasion of lymphatics of falciform ligament from epigastric peritoneum. Sometimes from hepatic metastases	5	9
Gall-bladder or ducts	If on fundus, by contact with epigastric peritoneum. If at neck by extension of permeation from portal glands	4	8
Spleen	Situated not very far from the infected epigastric peritoneum ...	2	4
Ovaries	From cancerous particles which fall into the pelvis.	6	11
Pelvic peritoneum...		3	6
Fallopian tube ...		1	2
Surface of uterus...		1	2
Mesentery	From the dispersion of cancerous particles through the peritoneal cavity.	3	6
Peritoneum generally		2	4
Intestinal peritoneum		2	4
Lumbar glands ...	By secondary embolic gland-infection from the other abdominal metastases in the later stages of the disease.	5	9
Lumbar vertebræ...		1	2

The Hepatic Metastases following Epigastric Invasion.

When a breast-cancer has penetrated to the epigastric peritoneum the liver may be attacked in two distinct ways. Free cancer cells may implant themselves on its surface, or permeation may pass along the lymphatics of the falciform ligament to the portal glands, and thence secondarily extend against the lymph current into the interior of the liver. In the latter event there is not necessarily any evidence of the escape of cancer cells into the peritoneal cavity.

In dealing with this question we will consider, for the sake of simplicity, only those cases in which the liver alone of the viscera had been attacked. There were 36 such cases, divisible into three classes:— (*a*) those in which the hepatic infection is local and limited, (*b*) those in which it is universal and advanced, (*c*) those which cannot be classified owing to the absence of detailed information.

Thirty-six Cases of Pure Epigastric Invasion in which the Liver was the only Organ infected.

Class (A).—Local and Limited Hepatic Infection, Fourteen Cases.

In five cases there was a single nodule on the liver—G. 141, 84, M. 94, 72 (near the gall-bladder). M. 263, 82. M. 41, 83, M. 26, 92.

In three cases there were two nodules in the liver—G. 399, 74 (both on upper surface), M. 176, 82, M. 79, 91.

In six cases there were a few nodules, which in two cases were specially noted as being on its surface—G. 214, 77, G. 127, 80, G. 216, 85, M. 215, 79, M. 232, 85, M. 40, 98.

M. 215, 79 was specially interesting because the abdomen had been infected, while the axillary glands are noted as being free from growth. This is not a solitary case, *v.* G. 380, 91.

It seems certain, from my personal observation, and from a study of the few cases where details are given as to localisation of the hepatic deposits, that these localised deposits were on the convex surface of the liver. Proof, however, is wanting, for post-mortem records are usually silent on the point.

Class (B).—Extensive or Universal Deposits. Seventeen Cases.

In six cases there were "numerous nodules," or the liver was "studded with secondary deposits"—M. 66, 72, M. 104, 73, M. 17, 84, M. 240, 84, M. 138, 90, M. 163, 90.

In eight cases there was practically universal infiltration of the liver, or it was full of large nodules—G. 197, 82, G. 46, 85, G. 10, 94, M. 61, 72, M. 60, 74, M. 130, 76, M. 207, 76, M. 298, 99.

In the remaining three cases details are given as to the distribution of the deposits.

G. 455, 90, Liver weighs 54 oz. In the left lobe a solid white deposit on the convex surface.

G. 30, 91. About thirty white superficial nodules. Interior of liver fibroid, and shows numerous white new secondary growth.

M. 147, 93. Liver studded over with umbilicated nodules,

Class (C.)—No Details given as to the Hepatic Infection. Five Cases.

The precise distribution of secondary growths in the liver in breast-cancer will be best studied by such details as are available in the whole number of cases. The materials for the proper study of the localisation of hepatic secondary deposits in breast cancer are unfortunately lacking, because the attention of pathologists has not been directed to the question. Such evidence as there is points strongly to the conclusion that secondary deposits in the liver in breast-cancer very frequently make their first appearance on its convex surface near the falciform ligament. This conclusion accords with my personal observations, and points to epigastric invasion as the most frequent cause of hepatic deposits.

Primary Invasion of the Portal Glands through the Epigastric Parietes.

The portal glands often become cancerous as a *result* of hepatic metastases, but this is by no means invariably the case. Cancer of the portal glands may be the cause of hepatic deposits, as is shown by its occasional occurrence while yet the liver remains free from growth, The case I am about to relate illustrates this point.

A man, aet. 74, died of cancer of the left breast of eight years' standing. A year before death the axillary glands enlarged. Six months before death jaundice supervened. The only visceral deposits were a small mass of growth in the portal fissure surrounding the neck of the gall bladder, and a nodule in one portal gland.

Among the 53 cases of uncomplicated epigastric invasion, this case was the only one showing freedom of the liver from growth in the presence of cancerous portal glands.

It must, of course, be rare in cases where the chest is free from growth for the patient to die at such an early stage of the abdominal invasion. Such cases as the preceding therefore possess a value out of all proportion to the frequency of their occurrence. They probably represent a common class of case in an exceptionally early stage.

Some of the best instances of portal gland invasion in breast cancer are found among the cases where the primary growth has not only invaded the abdomen but the thorax also. Together with the case just quoted they conclusively prove that portal-gland infection may be the cause, and is not always the consequence of hepatic metastases.

In a total of 422 cases, along with thoracic deposits, abdominal metastases were found *exclusively* in the portal glands in two cases. In two other cases the portal glands were cancerous, while the liver had escaped invasion.

Lymphatic Connections of the Portal Glands.

The breast is indirectly connected with the portal glands by two routes:—

(*a*) Certain efferent lymphatics originate upon the anterior part of the convex surface of either lobe of the liver, and thence pass into the falciform ligament at the level of its attachment to the abdominal wall. They curve downwards and backwards, and entering the umbilical notch above the round ligament, they pass backwards in the umbilical fissure to the portal glands. The connexion of these lymphatics with the subserous lymphatic plexus in the epigastric angle and thence through the linea alba, via the fascial plexus, with the mammary lymphatics, was demonstrated in Case III. Chapter V.

(*b*) Several efferent lymphatics run forward along the umbilical fissure from the portal glands. Turning upwards at the umbilical notch they pass between the layers of the falciform ligament to pierce the diaphragm, and terminate in glands lying on its upper surface to the left of the middle line between the pericardium and the anterior wall of the chest. Efferent lymphatics pass from these glands to the internal mammary chain, and so a connection is indirectly

established with the breast. Permeation may possibly extend from the breast to the portal glands by this route, but owing to the two sets of glands which have to be penetrated this must be a late event, and must be accompanied by advanced intra-thoracic growth.

Central Invasion of the Liver from Cancerous Portal Glands.

Sometimes the liver presents a large central mass of growth, while its periphery is relatively normal. In other cases the whole organ is enormously enlarged and cancerous throughout, and even under these circumstances, no metastases indicating the escape of cancer cells into the peritoneum may be present. These cases are best explained as due to permeation extending up-stream into the hepatic lymphatics from cancerous portal glands. The absence of trans-peritoneal implantation in such cases is at present unexplained.

It is possible that in some of these cases, cancer particles have been carried into the liver by the anastomoses which are known to connect its veins with those of the epigastric parietes, but for reasons already given this event is probably exceptional.

Infection of the Liver by Implantation from the Cancerous Epigastric Peritoneum.

It is, of course, not very common for a patient with breast-cancer to die at such an early stage of infection of the liver that it can be said with certainty in what way that infection occurred, so that the following cases have an importance out of proportion to their number :—

Case III, Chapter V.—The epigastric peritoneum was examined and proved to be cancerous ; Fig. 40 represents it. A few small nodules were visible on the convex surface of the liver on either side of the falciform ligament, none in its substance.

Case II, Chapter V.—The rectus muscle just below the ensiform cartilage was extensively infiltrated in its whole thickness (see Fig. 35). A large solitary nodule, represented in Fig. 32, was present in the liver at the umbilical notch.

G. 399, 74. Cancer of left breast. Liver fatty, weighs 63 oz. Two nodules on its upper surface—one on the surface of the right lobe, the other on that of the left lobe. No growth in the thorax, nor other metastases in the abdomen.

G. 127, 80. Cancer of right breast. The liver weighs 46 oz. and presents three small grains of cancer on its surface, and one 4 mm. in diameter, also superficial. No growth in the thorax, nor other abdominal metastases.

M. 40, 98. Cancer of left breast. The liver contains four nodules the size of a shilling. No growth in thorax nor other abdominal metastases.

It is unfortunate that, as a general rule, the records of autopsies do not give details as to the situation of secondary nodules in the liver. If they did I am confident it would be found that in a large proportion of the cases where only a few deposits are found in the liver, those deposits are situated on its convex surface in the neighbourhood of the falciform ligament.

Such deposits cannot easily be accounted for by blood-infection, and almost certainly arise in one of two ways, either by infection from the epigastric or from the subphrenic peritoneum. When the chest is free from growth the latter possibility may be excluded, even in the absence of a microscopic examination of the epigastric parietes.

It is hardly necessary to say anything about the further dispersion of cancer cells from the cancerous epigastric peritoneum in cases of epigastric invasion.

It may, however, be pointed out here, that the multiplicity of metastases in cancer of the breast, as compared with other forms of cancer, is largely due to its invasion of the abdominal cavity at its summit, where gravity affords the maximum of assistance in distributing showers of cancer cells over the various abdominal organs. The only primary growth starting low down in the abdomen which affects the liver with anything like the same frequency as cancer of the breast is rectal cancer. In the latter variety of growth, the rich plexus of haemorrhoidal veins affords every facility for the invasion of the liver by the blood-stream.

Pelvic Deposits in Cases of Epigastric Invasion.

In two out of 53 cases of pure epigastric invasion abdominal secondary deposits were present only in the ovaries. Among the eight cases of epigastric invasion showing multiple abdominal metastases (see Table V. on p. 124), in five cases growth in the liver was associated with pelvic growth. The frequency of ovarian metastases in breast-cancer is, of course, a well-known fact, for which, owing to the rich blood-supply of the ovary, the embolic theory provides a plausible explanation. But this view does not explain why the ovaries sometimes escape while other areas of the pelvic peritoneum show cancerous nodules as in the third case of Table V. In one fortunate case I was able to trace the earliest stage of pelvic invasion. The only visible pelvic secondary deposit in this case was a tiny miliary nodule, shown by the microscope to be cancerous, on the floor of Douglas's pouch. I believe that in nearly every case pelvic secondary deposits arise from the gravitation of cancerous particles into the pelvis, and their subsequent implantation on one or other of the pelvic organs. The ovary appears to offer the most favourable pelvic nidus for cancerous implantation.*

In the late stages of secondary pelvic growth the whole pelvis may be filled by cancer, and its contents matted together. Such cases may easily be mistaken for primary cancer of the rectum or the uterus, especially when the growth ulcerates through into one or other of these cavities. In view of these facts, recorded cases of double primary carcinoma of the breast and the uterus, or of the breast and the rectum, should be regarded with a critical eye.

Metastases in the ovary were present in 16 (4·8 per cent.) of the Middlesex Hospital cases, and in 8 (8·6 per cent.) of the Guy's Hospital cases, and in 5·6 per cent. of the whole number.

At first sight it is somewhat difficult to understand why infection of the ovaries should be found less frequently in an advanced than in a comparatively early set of cases. But it was found that the Guy's Hospital cases—cases which were

* See a clinical lecture on "Secondary (Metastatic) Carcinoma of the Ovaries," by Mr. Bland-Sutton, *Brit. Med. Journ.*, May, 26th, 1906.

willing to submit themselves to operation—have a much younger average age than the Middlesex Hospital cases, many of which were admitted in an inoperable stage. It seems likely that the more frequent occurrence of ovarian metastases in the former series simply shows that the ovaries form a more favourable nidus for growth before the menopause than after. Taking all the cases of breast-cancer 37 per cent. are found in patients under 50 at the time of their admission to hospital, and about 61 per cent. in patients over 50. On the other hand sixteen instances out of twenty-four of secondary growths in the ovaries occurred in patients under 50 at the time of admission. It appears, then, that ovarian metastases are three times more frequent before the menopause than after it.

This fact is no doubt connected with the atrophy and fibroid induration which occurs at the menopause, and renders the ovary less penetrable to the attacks of cancer.

The Symptoms of Epigastric Invasion.

I believe that it will sometimes be found possible to diagnose epigastric invasion when epigastric pain and tenderness are present even apart from hepatic enlargement or jaundice. Subcutaneous nodules in the epigastric region are probably an unequivocal indication that epigastric infection has occurred. But in a large majority of cases epigastric invasion takes place without the formation of any palpable nodules in the epigastric region. The nodules represented in the Frontispiece upon the anterior layer of the rectus sheath could not be detected clinically, yet in the case from which this specimen was taken epigastric invasion had occurred.

A vivid clinical picture of what I take to be a very acute case of pure epigastric infection is given by Mr. Henry Morris in a paper on cancer following Paget's disease.* Eczema of the nipple in this case dated from 1870.

> There was some ill-defined hardness in the substance of the left breast. At the site of the nipple was a depressed and foul ulceration; the upper border was slightly indurated and everted, the lower soft. There was some ill-defined induration in the breast. On August 30th,

* "On two cases of Carcinoma of the Breast, preceded by so-called Eczema of the Nipple and Areola" (*Med. Chir. Trans.*, vol. lxiii, 1880, p. 27).

1876, the breast and a large axillary gland were removed. She left the hospital well on October 3rd, 1876. In August, 1877 she gave birth to a healthy child. In October, 1877, she was taken ill with sickness, giddiness, and faintness, quickly followed by a severe pain at the pit of the stomach. Three days afterwards she felt a lump in the belly, near the pit of the stomach, from which sharp penetrating pains shot across the body and through to her back. The lump increased rapidly in size, she frequently vomited a greenish fluid, occasionally tinged with blood; and had repeated attacks of diarrhœa, attended with a bearing-down pain in the rectum. By the end of January, 1878, both the severity of the pain and the size of the tumour had much increased. The general surface of her body was slightly jaundiced, the face and conjunctiva still more so. As she lay on her back a large tumour, intensely hard to the touch, was seen extending across the right hypochondrium and the umbilical regions, the border of which presented very prominently against the abdominal walls. Some nodules of bony hardness could be felt over other parts of the abdomen, and a wave of fluid was distinctly displaced by the fingers from between the abdominal wall and the surface of the enlarged liver. The cutaneous veins of the abdomen were much enlarged. A flat, indurated growth, the size of a crown piece, occupied the middle of the scar in the left mammary region.

The axillary glands were unaffected . . . She was again admitted into the hospital, and died seven days afterwards.

At the post-mortem examination, which was made by Dr. Coupland, the peritoneum was found extensively studded with firm, cancerous nodules; much bile-stained fluid in the peritoneal sac. The liver was enormously enlarged, especially its right lobe, and weighed 108 oz.; its surface was uneven and nodulated and its capsule thick, rough, and opaque. On section its substance was extremely firm, of the consistence of gristle, and was pervaded by tough, gristle-like nodules, whitish, ill-defined, and mottled with patches of orange-coloured pigment. Spreading out in all directions around the nodules similar material infiltrated the hepatic tissue, the lobulation of which was very ill-defined. There were some hard, whitish, flattened nodules in the falciform ligament.

In Dr. Goodhart's opinion, the portal canals were evidently the route by which the cancer spread into the liver. It was probably, therefore, attacked by permeation from the portal glands.

In the second case recorded by Mr. Morris in the same paper, a small cord-like projection made its appearance just below the xiphoid cartilage three months before death. This would appear to have been a fascial nodule of growth. Soon afterwards epigastric pain, slight at first, but increasing

in severity, and associated with epigastric tenderness, made its appearance. The liver was found to be considerably enlarged, more especially in the epigastric portion. When the patient died a few weeks later, the liver was extensively infiltrated with cancer and weighed ninety ounces. The lungs showed peri-bronchial and sub-pleural infiltration, and a few isolated cancerous nodules. Both suprarenals contained cancerous deposits.

Epigastric tenderness appears to be a frequent symptom. It was recorded by Mr. T. W. Nunn* as far back as 1873, in a case where, after death, the liver was extensively cancerous and the thoracic organs free from growth—evidently a case of pure epigastric invasion.

* Nunn, "Two Cases of Cancer of the Left Breast" (*Clin. Soc. Trans.*, 1873).

CHAPTER VII.

VISCERAL DISSEMINATION (continued): RETRO-PERITONEAL AND DIAPHRENIC INVASION OF THE ABDOMEN. INVASION OF THE THORAX AND OF THE CRANIAL CAVITY.

Retro-peritoneal Invasion of the Abdomen.

When cancer-cells obtain access to the pleural cavity—a frequent event—they tend, under the influence of gravity, to implant themselves especially about the lower limit of the posterior parietal pleura, at the lowest point of the pleural cavity. Permeating the sub-pleural lymphatic plexus, they soon reach the lymphatics of the diaphragmatic crura. This is an event of great importance, for the crural lymphatics, unlike those of the rest of the diaphragm, do not carry lymph to the thoracic glands, but drain into the lumbar glands of the abdomen. Among the 115 cases which showed a single abdominal secondary deposit, there were ten in which the solitary metastasis was situated in the kidneys, the suprarenals, the lumbar glands, or the lumbar vertebrae. These organs, and the posterior portion of the liver, suffer in retro-peritoneal invasion, and they may be found embedded in a mass of diffuse growth which is replacing the perirenal fat. Trans-peritoneal implantation, if it occurs at all, is a very late event. In one case among the Guy's records the pathologist describes this process as follows:—"The disease had travelled by the lymphatics through the left crus of the diaphragm; lying upon this crus was a cancerous gland the size of a filbert; a chain of cancerous glands, none larger than this, could be traced down the front of the spine to the pelvis, and also to the portal fissure." The primary growth was in the left breast, and there were deposits in the left pleura. Considerations of space forbid me to describe the case, in which I was able microscopically to confirm these observations.

But this is not the only way in which retro-peritoneal invasion may occur, for in six cases, all of them, be it noted, occurring in the late (Middlesex Hospital) series, retro-peritoneal invasion was found in the absence of thoracic invasion. In three of these six cases subcutaneous nodules were present —a very high proportion, for they were found in only 3 per cent. of the early and in 22 per cent. of the late series. Subcutaneous nodules are an index of extensive permeation of the fascial lymphatic plexus, and it seems probable, in the cases in question, that this process had extended to the loin, and thence by way of the intra-muscular lymphatics to the perirenal fat and the lumbar glands. In one case, at a point just below the twelfth rib, I traced a longitudinally-cut permeated lymphatic for some distance into the underlying muscles from the invaded fascial plexus; and it is to be noted that the parietes in this region are comparatively thin.

The rarity of retro-peritoneal invasion in the early series of cases shows that it is a very late event, whose only importance is that it may give the *coup de grâce* to an already doomed patient. It must always be preceded either by thoracic invasion or by very extensive parietal dissemination.

Since the preceding account of retro-peritoneal invasion was written, Tendeloo * has independently made similar observations on invasion of the retro-peritoneal lymph-glands, not only in cancer, but in other morbid conditions of the thorax. In several cases of empyema and pyopneumothorax he found suppurating glands along the abdominal aorta, but nowhere else in the abdomen. In intra-thoracic tuberculosis he has found these glands tuberculous when all the other abdominal glands were free.

He investigated the distribution of the metastases in four cases of mammary cancer, in all of which the chest wall was penetrated by growth; there was lymphangitis carcinomatosa in the lungs, and metastases were present in the mediastinal glands and in those lying on the diaphragm. On the diaphragm itself there was lymphangitis carcinomatosa.

* Tendeloo, "Lymphogene retrograde Metastase von Bakterien, Geschwulstzellen und Staub aus der Brust in der Bauchhöhle besonders in para-aortalen Lymphdrüsen."—Münch. Med. Wochenschrift, Aug. 30th, 1904.

As regards the condition of the abdominal organs :—

Case 1. No metastases.

Case 2. Metastases in one pre- and one retro-aortal lymph gland.

Case 3. A nodule in the liver immediately under the convex surface, and metastases in the para-aortal lymph-glands as far as the bifurcation of the aorta.

Case 4. Metastases in the liver and in the portal glands.

The author proceeds :—"One cannot assume at once that, while all the thoracic metastases have occurred along the lymph-channels, the closely-associated metastases in the abdominal organs have occurred along the blood-vessels. The fact that these abdominal organs, including the liver, are connected immediately by lymphatics with the intra-thoracic lymphatics, and the position of the metastases, speak for a dissemination by way of these lymphatic channels."

Tendeloo in a number of cases confirmed these observations by finding dust, similar to that which occurs in the bronchial glands, in the para-aortal lymphatic glands, but nowhere else in the abdomen. He inferred that it had passed by the lymphatics from the chest to the abdomen, though he failed to find it in the diaphragm itself (except in one case). He adduces weighty arguments in support of this view.

Tendeloo believes that adhesion of the lungs to the diaphragm plays a part in producing the retrograde stream of lymph, which in his opinion is responsible for the infection of the para-aortal glands by bacilli, cancer-cells, or dust.

Tendeloo's fourth case, in which cancerous portal glands were present, is important because he found the retro-peritoneal glands at the same time normal. His investigation was specially directed to the latter set of glands, so that his negative statements with regard to them may be implicitly accepted. The case strongly confirms my views on epigastric invasion, for it shows that the earliest lymphatic deposits in the abdomen may be found in the portal glands.

Diaphrenic Invasion of the Abdomen.

In rare and late cases the abdomen may be invaded from the thorax by direct infiltration of the substance of the

diaphragm in its anterior part. The best-described case of this kind occurs in the records of Guy's Hospital:—

Necropsy, No. 164, 1882, Guy's Hospital.—The right breast was represented by a sound operation scar, though there was growth in the intercostal spaces beneath. The primary growth had spread down the anterior parietal pleura, which towards its lower part formed a thick plaque of growth, to the diaphragm. It had infiltrated the tendinous part of the diaphragm. The liver had become adherent to the under surface of the diaphragm, and was being invaded by growth like dense scar tissue, puckering the upper surfaces of the liver, and extending by bands into its structure. As a secondary result, numerous white translucent nodules of cancer were scattered throughout the liver, both within and on its surface. None of these were umbilicated.

In this case diaphrenic infection had got a long start of retro-peritoneal infection. The commencement of the latter was probably indicated by the presence of one or two nodules in the right, and one in the left, suprarenal. The primary growth was in the right breast, and there was 30 ozs. of blood in the right pleura, which had been tapped just before death.

The transperitoneal implantation which almost necessarily follows diaphrenic infection had not in this case made much progress. It was indicated only by the presence of many translucent white nodules of growth, some only just visible to the naked eye, others as large as a pea, which were scattered over the great omentum. The presence of adhesions about the liver had apparently interfered with the dissemination of cancer-cells through the peritoneum. The adhesion of the great omentum to the internal ring of an inguinal hernia may also have protected the viscera lying behind it.

Cancer, like empyema, appears to find great difficulty in penetrating the diaphragm from above downwards, perhaps on account of the exceptionally strong lymph-stream which is opposed to it. The diaphragm is recorded as the seat of cancerous deposit only six times in 422 autopsies. In a case which I was able to examine microscopically, the anterior part of the diaphragm formed an indurated sheet 6 mm. thick. The layer of growth lay entirely on the pleural aspect of the diaphragm, and had only partially infiltrated the underlying muscle and tendon. The subphrenic peritoneum, normal to the naked eye, showed early microscopical infiltration. The lymphatics of the falciform ligament were permeated, but, nevertheless, the liver was free from cancer. An extensive mass of retro-peritoneal growth was present. This case

illustrates the extreme lateness, and consequent rarity, of diaphrenic invasion. For retro-peritoneal invasion—itself a late event—was present in an advanced degree, yet diaphrenic invasion was still in the earliest stage.

The abdominal course of diaphrenic invasion must be exactly similar to that of epigastric invasion, for in both cases the cancer-cells reach the peritoneal cavity at about the same point, though by different routes.

Invasion of the Thorax.

Since the modern operation for breast cancer appears to afford all the security against thoracic invasion which it is possible to attain, I have not paid much attention to this subject. There are, however, one or two points to which attention may be called. That obliteration of the pleural cavity delays the course of dissemination is, I believe, a new observation, not devoid of therapeutic suggestions.

Invasion of the Anterior Mediastinal Glands.

It is sometimes stated, or implied, that some of the lymphatics of the breast convey lymph, not to the axillary, but to the anterior mediastinal glands. And it is doubtless true that there is a mediate communication between the breast and these glands by way of the pectoral lymphatic plexus, and of the perforating branches which run from that plexus to the glands in question. These perforating branches must, however, be regarded, not as true afferent lymphatics, but as mere anastomotic channels of small diameter and sluggish stream, along which embolic transport of cancer-cells cannot occur. How otherwise can the comparative immunity of these glands be explained?

Invasion of the axillary glands is an early and almost constant event. In the anterior mediastinal glands, on the contrary, Török and Wittelshöfer,* of 366 autopsies, found cancer in only 6·5 per cent. Permeation appears to be the only process by which breast cancer can reach these glands, and their comparative immunity shows either that it reaches them late, or that they are able to destroy the comparatively

* Török and Wittelshöfer, "Arch. fur klin. Chirurg.. Bd. xxv., 1881," p. 873.

limited number of cancer-cells which can in this way reach them. These perforating branches, guarded as they are by glands, are probably far less dangerous than the fine direct communications which, according to Roger Williams,* connect the pectoral lymphatic plexus directly with that of the pleura. There is a considerable body of evidence that lymphatic glands are able to deal with cancer-cells in limited doses; Williams especially has drawn attention to the fact that, in days when the axillary glands were not removed with the breast, axillary recurrence was not so frequent as, with our present microscopical knowledge of axillary gland invasion, we should expect to find it.

In this connexion it is perhaps worth recording that in a case of diaphrenic invasion of the abdomen, I found in the interspace between the seventh costal and ensiform cartilages, embedded in the tissues, one or two minute nodules of lymphoid tissue containing cancer cells. It is possible that these nodules, which are not constantly present, had in this case protected the abdomen against epigastric invasion, and had thus given time for diaphrenic invasion to take place.

Trans-pleural Implantation.

The pleural cavity is most frequently invaded by direct infiltration of the thoracic wall beneath the primary growth. Not infrequently, I think, cancer-cells obtain access to it at its apex by cancerous infiltration around infected supraclavicular glands.

The importance of the escape of cancer-cells into the pleural cavity, and of subsequent trans-pleural implantation, is shown by the great frequency of secondary growths of the pleura. They occurred in 38 per cent. of 422 cases. Sometimes, as in a specimen which illustrated my "Astley-Cooper" Prize Essay, secondary growths of the pleura may assume a polypoid form, and may hang into the cavity by delicate non-cancerous pedicles. In such a case transpleural implantation is seen in an unmistakable form. So far as my observation goes, implantation growths are nearly always most abundant near the bottom of the pleural cavity, though they rather avoid the diaphragmatic peritoneum. Post-mortem records

* Roger Williams, "Diseases of the Breast," p. 181.

give little information on this subject, an omission to which attention may be called.

Invasion of the Lungs.

The lungs showed metastases in only 25 per cent. of all cases. As a general rule they are invaded by permeation, which extends into them either from the pleura or from cancerous bronchial glands. It is rather the exception to find nodular deposits, such as might be supposed to result from embolism.

The Protective Influence of Pleural Adhesions.

If trans-pleural implantation is an important process, it should be possible to show that obliteration of the pleural cavity checks dissemination to an appreciable extent. The most convincing evidence on this point will naturally be derived from the late (the Middlesex Hospital) set of cases. Marked pleural adhesions were present in thirty-seven of the 329 cases. Cancerous invasion of the pleura was present in only eleven (30 per cent.) of these thirty-seven cases, while of the sum total of Middlesex Hospital cases, 44 per cent. showed pleural invasion. In three of these eleven cases the adherent pleura on the side of the growth had escaped invasion, while the opposite non-adherent pleura was cancerous.

Doubt may at first sight appear to be thrown on this evidence of the protective action of an adherent pleura by the fact that only 30 per cent. of the cases with pleural adhesions were absolutely free from metastases, as compared with 33 per cent. of the sum total of cases. But the protective action of an adherent pleura extends only to the thoracic cavity. It has been shown that in a large proportion of cases invasion of the abdomen occurs, not by way of the thorax, but directly through the epigastric parietes. Pleural adhesions do not check this process—perhaps, indeed, their resistance to the deep extension of the growth may accelerate the progress of fascial permeation, and so actually favour epigastric invasion. It is a most striking fact that 32 per cent. of the thirty-seven cases with marked pleural adhesions, showed the abdomen invaded by cancer and the chest free, while only 12 per cent. of a total of 329 cases showed a similar state of affairs.

The converse difference is equally striking. While 22 per cent of the Middlesex Hospital necropsies show the thoracic cavity invaded and the abdomen free, only 5 per cent of the cases with pleural adhesions show a similar state of affairs. These facts are a strong indirect testimony both to the frequency of epigastric invasion, and to the protection afforded by pleural adhesions to the thoracic cavity. Incidentally they provide a strong argument against the embolic theory, by showing that invasion of the abdomen and invasion of the thorax are independent events.

Secondary Deposits in the Brain.

No doubt deposits in the brain frequently, though not necessarily (see p. 37), indicate infection by the blood stream. They were found in sixteen cases, that is in nearly 4 per cent of all cases. In only one of these cases did death result shortly after operation ; there is, therefore, no evidence that operation can set up a blood-infection comparable to the general tuberculosis which sometimes follows operation on tuberculous lesions. In three cases no details are given as to the distribution of the deposits. They are found most frequently in the cerebellum (seven cases). Of these, three were in the right lobe and two in the median lobe, while in two the distribution is not given. Next to the cerebellum come the frontal lobe and the parietal lobe, each affected in five cases. The deposits were bilateral in one case in each of these lobes. Two cases showed deposit in the right frontal lobe, and two in the left frontal lobe, two cases in the right, and one case in the left, parietal lobe. The basal ganglia were affected in three cases, the right occipital lobe once, and the left island of Reil once.

Apparently, secondary growths of the brain have some preference for the right rather than the left lobe of the cerebellum.

Since the brain not infrequently escapes examination, it is probable that secondary cerebral growths in breast-cancer are commoner than statistics would indicate.

Secondary growths in the brain were only found in one of the cases included under the heading "Death after Operation

or from Intercurrent Disease." This appears to show that they are always late in making their appearance, and bears out the view that blood-infection is a late or terminal event.

Secondary Deposits in the Dura Mater.

These were found in nine (2·7 per cent.) of the Middlesex cases, in three (3·2 per cent.) of the Guy's cases, and in about 3 per cent. of all cases. Probably they frequently escape notice because the skull is not opened.

I believe they frequently arise from without by penetration of the bone from cancerous permeation of the lymphatic plexus of the scalp. This view is borne out by the frequency of their association with subcutaneous nodules, which were found in six out of these twelve cases. The average frequency of subcutaneous nodules is only one case in five. The brain may be free from growth when the skull and dura mater show deposits.

Deposits in the dura mater may, however, be secondary to deposits in the brain, the result of blood infection.

Evidence for the Permeation Hypothesis in the Pathological Records of Breast-Cancer.

If the permeation hypothesis of dissemination is true, it should be possible to find some evidence in its favour among recorded cases of breast cancer which have been submitted to careful and systematic microscopic examination. As a rule, however, the histological examination is confined to a small piece of the primary growth, and to an axillary gland. I have found only one case in which an adequate attempt was made to unravel by the aid of the microscope the tangled problem of dissemination. A brief abstract of the record of this case will be of interest.

A. F., single, aet. 40 * noticed in May 1890 a tumour in the left breast. The lump did not increase in size after it was noticed, but became harder and less movable. It was found after death to be a fibroma †. In October 1892 she noticed many new shotty, painless

* Bramwell and Leith, *Edin. Med. Journ.*, July and Aug. 1894.

† This may be an instance of a primary carcinomatous growth undergoing complete fibrosis—the cancer cells being strangled by their stroma.—W. S. H.

lumps in both breasts, and in the skin on the front of the thorax and abdomen. Diplopia and blindness in the right eye now came on, and she suffered from pain in the left hip.

On admission in January 1893 both breasts were infiltrated with innumerable hard pea-like nodules. Numerous nodules spread out from each breast in radiating chains. Some of these chains ran almost up to the clavicle, others passed towards the axillae, others towards the middle line, and a few ran down towards the abdomen. Several isolated nodules lay in the subcutaneous tissues on the front of the chest and abdomen; a group of nodules was situated round the umbilicus; there were a few in each axilla, several on each side of the neck, many in each groin, and one behind the left ear at the junction of the skin with the scalp. There were no nodules in the flexures of the nams or elbows. All the nodules were freely movable and covered by normal skin. A nodule removed for examination showed the character of scirrhous cancer. The liver and spleen were smooth and enlarged, extending downwards to the umbilicus. In Feb. 1893, on vaginal examination, several small nodules, like those beneath the skin, were felt in the upper part of the vagina. In March the breast nodules were becoming more numerous. In April the upper part of the left femur was found to be enlarged, nodulated, and tender on pressure. Several small subcutaneous nodules developed over the back of the trunk. The patient died on May 1st, 1893.

The autopsy showed that the mesentery and peritoneum were thickly studded with small nodules. The liver was smooth on the surface, and studded throughout with small nodules; the whole substance of its left lobe seemed uniformly infiltrated, while in some parts of the right lobe the nodules were more isolated.*

The spleen, ovaries, kidneys, and adrenals showed nodules, mostly lying just beneath their capsules. The pancreas showed one nodule, the stomach three nodules. The parietal and visceral pericardium and pleurae showed nodules. The substance of the lungs was free from metastases (a fact difficult to explain on the embolic theory). The dura mater was thickened and infiltrated by numerous cancerous nodules. The brain itself was healthy. The upper third of the left femur was invaded throughout by cancerous nodules.

An exhaustive microscopic examination of the case was made by Dr. R. F. C. Leith.

The cells of the carcinoma were unusually small, with very little protoplasm and large clear nuclei. Their appearance indicated rapid growth and a proneness to degeneration. The following details

* Since only the left lobe of the liver lies in direct contact with the epigastric parieties, it frequently happens in cases of epigastric invasion, that the left lobe shows more extensive cancerous deposit than the right one.—W. S. H.

extracted from the report, appear to me to show, quite apart from the centrifugal mode of spread shown by the clinical history of the case, that the cancer extended by permeation, i.e. by actual growth along the lymphatic vessels.

The lymphatics of the visceral (and parietal) pleura were extensively and apparently universally filled with cancer-cells. Around the lymphatics, at close intervals, were little areas of cancerous growth. The cancerous infiltration showed some tendency to pass along the lymphatics of the interlobular septa, but encroached only slightly on the lung substance. Here and there small haemorrhages had taken place into the cancerous lymphatics. No cancer-cells were seen in any clearly recognisable pulmonary blood vessel.

There was a general cancerous infiltration of the lymphatic and tissue spaces lying between and around the fat-cells of the deeper layer of the epicardium.

In the liver the lymphatics of some of the portal spaces, especially around the portal veins, were engorged with cancer-cells. In Dr. Leith's opinion the hepatic metastases were too extensive to be accounted for by lymphatic distribution, but he does not record the presence of cancer-cells in any of the blood vessels.

The sub-capsular lymphatics of the spleen were pretty generally filled with cancer-cells. Some of the larger veins of the splenic pulp appeared to contain small cancer-cells.

Close to the internal surface of the cancerous dura mater, a few large sinuses filled with blood were seen lying among cancer-cells.

From this careful research Dr. Leith came to the following conclusions. As regards the breast itself :— "The primary nodule or nodules had thus given rise to secondary and separate nodules in the same organ by a true metastasis which was mainly, if not entirely, by means of the lymphatic vessels, These were seen microscopically to contain cancerous plugs. partially filling them, and it is possible that some unusual particulate or chemical irritant derived from the cancerous growth, in its course along the lymph-stream in advance of the cancer-cells, set up an irritation of the endothelial lining of the lymphatic vessels, causing some alteration in them which favoured the frequent and abundant settling down of cancer-cells upon their walls, and that such cancerous thrombi formed the nuclei of new nodules." Dr. Leith thus, if I understand him aright, regarded the normal or reversed lymph-stream as the agent which disseminated cancer-cells along the fine lymphatic vessels of the breast.

As regards the cancerous invasion of the lymphatics of the pleura, Dr. Leith thought it probably secondary to cancerous embolism of the pleural branches of the bronchial arteries. He also ascribed the other visceral metastases to embolic arrest of particles carried by the blood stream. But apart from the difficulties attending this explanation, already pointed out in Chapter I., Dr. Leith's most careful microscopical examination failed to produce satisfactory evidence of cancerous invasion of the blood vessels. On the contrary, it supplies, in my opinion at least, strong confirmatory evidence of the permeation hypothesis of dissemination — evidence whose value is considerably increased by Dr. Leith's bias in favour of the embolic theory.

CHAPTER VIII.

THE PATHOLOGY OF CANCEROUS PACHYDERMIA (SO-CALLED CANCER "EN CUIRASSE").

CANCER *en cuirasse* was first fully described by Velpeau in 1838 in one of the most vivid of his clinical word-pictures (see p. 17). Long before Velpeau's time, however, in 1792, Mr. Howard, the organizer of the Middlesex Hospital Cancer Wards, had described a case of the condition without attaching to it a special name.*

This terrible sequela of breast-cancer is at present considered to be a cancerous infiltration of the skin, due to the spread of the disease along the deep cutaneous plexus of lymphatics, a belief which appears to be quite erroneous.

Erichsen,† speaking on this subject, says:—

"The cancerous infiltration rapidly spreads into the surrounding integument, which early becomes contaminated, assuming a hard leathery character, or feeling brawny and infiltrated; often without discolouration, but presenting a hypertrophied appearance, the pores being enlarged and the interspaces between them increased. In other cases the infiltrated skin assumes a brownish or purplish colour, and is covered by rough desquamating crusts so as to resemble the bark of an old tree. . . . . I have in this way seen the integuments of the whole front of the chest, from the clavicles to below the mammae, and from one axilla to the other, infiltrated, hard, and leathery; of a brownish colour, forming a stiff cuirass, as it were, but without ulceration."

Prof. Watson Cheyne thus describes the condition ‡:—

"In other cases, preceding the actual adhesion of the cancerous tumour to the skin, the skin over the part may become oedematous

* "The Plan adopted by the Governors of the Middlesex Hospital for the relief of persons afflicted with Cancer." Quoted on p. 346 of the Sydenham Society's translation of Velpeau's "Diseases of the Breast," by Mr. Mitchell Henry, formerly Assistant Surgeon to the Middlesex Hospital.

† Erichsen, "The Science and Art of Surgery," 10th Edition, Vol. II., p. 796.

‡ Treves, "System of Surgery," Vol. II., p. 814.

and red without, so far as the microscope shows, any actual cancerous affection. Usually, however, such a condition precedes the diffuse development of cancer in the skin, the condition spoken of as *cancer en cuirasse*. In this form of disease the skin over the cancer, in the first instance, becomes hard, brawny, and red from diffuse infection of the lymphatic system of the skin with cancerous material, and this brawny condition may rapidly extend over the whole of the side of the thorax without any ulceration in the early stage. In other cases the affection of the skin is not due so much to direct spread of the original cancerous tumour to the skin as to the development in it of numerous nodules, probably from the cancerous material being conveyed along the lymphatic vessels in the suspensory ligaments, and affecting the deep cutaneous plexus of lymphatics. This condition, where numerous nodules are found in the skin over cancer of the breast, generally also ends in cancer *en cuirasse*. Very often in these cases the primary tumour is small, and belongs to the type of atrophic scirrhus. It is often situated under the nipple, and cannot be felt on account of the thickened leathery condition of the skin."

In considering these descriptions, there are certain facts to be especially noted as discordant with the current hypothesis. The skin may simply present the appearance of hypertrophy. Unlike the hard infiltrated skin sometimes seen at the edge of an ulcerated carcinoma it may be tough and leathery, with obviously enlarged pores, or covered with crusts like the bark of an old tree. These are not the characters of a tissue infiltrated by cancerous epithelium ; they are exactly the appearances seen in elephantiasis due to lymphatic obstruction, whatever the cause of that obstruction may be. Furthermore, we have it on Prof. Cheyne's authority, that in the prodromal stage of cancer *en cuirasse*, the microscope may fail to show any cancerous infiltration of the thickened skin.

It is very difficult to explain these facts upon the view that cuirass-cancer depends upon a cancerous invasion of the deep lymphatic plexus—a plexus whose very existence is, as we have seen (p. 47), extremely doubtful. Cancer infiltrates the tissues of the skin slowly and with difficulty. Although I have examined a number of sections of skin in the neighbourhood of breast cancer, I have never seen cancer permeating the supposed deep cutaneous plexus. The dermis in the

region surrounding a subcutaneous nodule is often practically not infiltrated by growth at all.

In one of my sections the edge of an ulcerated primary growth of the breast is extending underneath much-thickened skin in the fatty tissue. Even here the boundary between the dermis where it has been absolutely destroyed by the ulcerating growth and the thickened but non-cancerous dermis, is not a wide region showing spreading lymphatic infection, but an absolute line.

Clinically it appears quite certain that extensive spread of growth just under the dermis would soon be followed by extensive ulceration. But in cancer *en cuirasse* the skin, far from being ulcerated, is characterised by its leather-like rigidity and thickness. If ulceration does occur, it is a very late event.

The fact is that cancer *en cuirasse*, so far as it concerns the skin, is in its earlier stages essentially a non-cancerous condition, identical with the pachydermia which is seen in elephantiasis Arabum, and in some cases of long-standing eczema, and dependent on the same cause, obstruction to the return of lymph from the skin. Later on it is usually complicated by nodular cancerous invasion of the skin.

The swelling of the arm in breast cancer on the affected side, with brawny thickening of the integuments, is a less marked example of a very similar condition. Here it has never been suggested that the skin of the arm is infiltrated by cancer.

Oedema of the Arm on the side of the Primary Growth.

Oedema of the arm was found in 5 per cent. of the Guy's series and in 16 per cent. of the Middlesex cases. It is obviously therefore a late event.

Nunn* regards the oedematous arm of breast cancer as due to obstruction of the main lymphatics by growth within them, and not to compression by growth outside them. He points out that the axillary veins may be seen completely enveloped in a cancerous mass, and yet the arm may not be swollen.

* "Cancer," by T. W. Nunn, p. 23. Glaisher, 1899.

Both in cancer *en cuirasse* and in the brawny arm of breast cancer there is an early stage, characterised by swelling which pits on pressure, and often by redness; and a later stage characterised by thickening and brawny hardness.

Ziegler* describes two microscopical types of skin-affection in elephantiasis. The first apparently follows inflammatory affections, and is characterised by the formation of tissue akin to granulation tissue. In it the lymphatics and the tissues round them are full of lymphoid cells. In the second variety, which appears to follow lymphatic obstruction without inflammation, "the tissue is in many cases poor in cells and coarsely fibrous in texture, giving the impression that the normal fibrillae are not so much increased in number as in individual thickness." This description, with the addition that the lymphatics were distended by round cells, exactly fits the microscopic appearances presented by the skin in the following case of early cancer *en cuirasse* :—

Case of Early Pachydermia in Association with Breast Cancer.

Emily S., aet. 54, was admitted into the Middlesex Hospital in 1903, under Mr. Pearce Gould, with a hard carcinoma of the left breast. The growth had been present for three years, and ulcerated six months before admission. It was not fixed to the pectoral muscle. The nipple was retracted and large glands were present in the left axilla.

Upon section of the breast after its removal by operation, the grey, hard growth at the edge of the ulcer was seen extending for about half an inch beneath the skin in the subcutaneous fat. The growth was sharply defined, and beyond its edge the subcutaneous fat was normal. Upon the skin surface a broad tongue of white thickened skin was seen extending about three inches from the edge of the ulcer to merge in the healthy surrounding skin.

The only piece of tissue available for further examination was a strip of the skin and subcutaneous fat extending from the edge of the ulcer through this thickened area of skin. The strip did not reach as deeply as the pectoral fascia, the condition of which could therefore not be determined.

The thickened skin did not show the naked-eye characters of infiltration by carcinoma. It was white, firm, and rubbery, contrasting in this respect with the stony hardness of the primary growth. It was no less than 6 mm. thick. The boundary between the ulcerated

* Ziegler, "Pathological Anatomy, 1884," par. 396.

growth and the contiguous thickened skin was a sharp line, not a wide zone infiltrated by cancer. Microscopically the thickened skin, even close to the edge of the cancerous ulcer, showed no infiltration by cancer cells. The hypertrophied dermis consisted simply of fibrous tissue without any increase of nuclei or sign of inflammation. In the neighbourhood of the blood-vessels, however, were seen closely-packed collections of round cells (see Figs. 41A & 41B) such as are described by Ziegler in some varieties of pachydermia as indicating lymphatic obstruction.

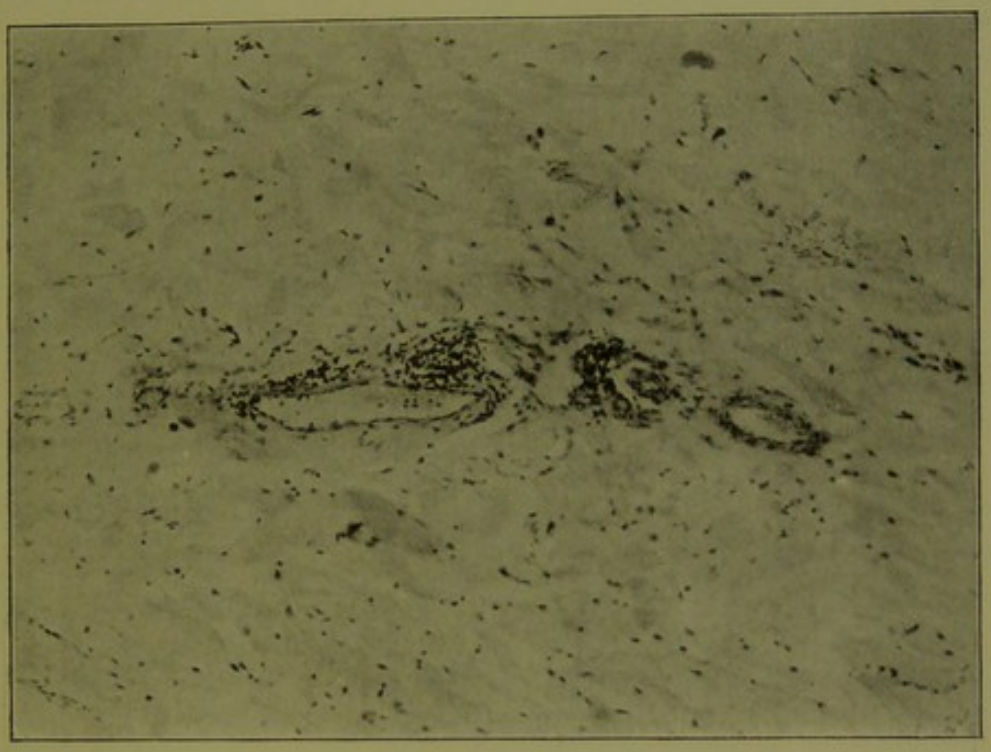


FIG. 41A.

Showing the microscopic characters of the dermis in cancerous pachydermia (early "cancer en cuirasse"). The dermis is very much thickened and swollen, and hyaline in appearance, but there is no increase of the nuclei, nor are cancerous elements present. The lymphatics, however, are crowded with small round cells, which are also numerous in the immediate neighbourhood of the blood vessels. There was also a slight round-celled infiltration of the superficial layers of the dermis. The whole thickness of the skin (6 mm.) is entirely free from growth.

In this case the thin skin of the female breast had attained a thickness only found normally in the thickest portion (dorsal region) of the skin of the male subject, and yet it showed no cancerous infiltration whatever, while presenting the typical characteristics of pachydermia.

Case of Late Pachydermia associated with Breast Cancer.

Constance C., aet. 57, was admitted into the Cancer Wards under Mr. Pearce Gould on Jan. 9th, 1903, and died of cancer of the left breast on Oct. 10th of the same year. A lump had been noticed in the left breast in 1901, but no operation was performed then or later. From one point of view the case has been already described in Chapter V. (Case III. of Epigastric Invasion). The left breast was completely atrophied, and was represented by a flat, warty, and ulcerated area

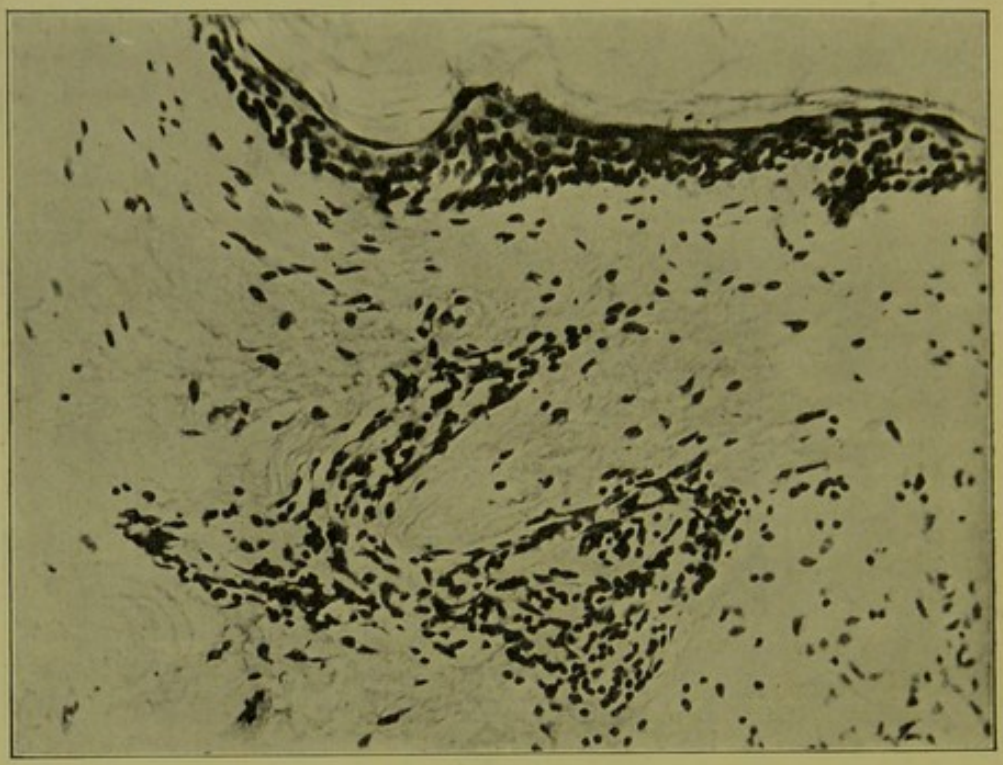


FIG. 41B.

A portion of the pachydermatous skin from the same case, under a higher power. This section shows the obliteration of the papillæ which accompanies the great thickening of the dermis. The section has passed through a sebaceous gland, and the lymphatic network around it is crowded with round cells. No cancerous elements are present. The cells of the normal sebaceous and sweat glands stain very deeply, and may sometimes have been mistaken for malignant epithelium.

puckering the surrounding skin, which showed cuirass cancer covering the left half of the thorax. The greater part of the pectoralis major muscle was atrophied, and the small portion of it remaining towards its insertion was hard and infiltrated by growth. The tissues in the axilla were matted and adherent, and there was slight swelling of the left upper arm. No enlarged glands were palpable in the neck.

The four slides now to be described showed the conditions present at various points, within the area of cancer *en cuirasse* :—

Slide 1.—A section of the skin and underlying tissues on the affected side, close to the middle line and at the level of the fourth costal cartilage.

The epidermis is thin and atrophic, and the papillae are atrophied. In places there is round-celled infiltration of the superficial layer of the dermis.

The deepest parts of the section consist of dense fibrous stroma containing closely-packed cancer-cells. On the other hand the superficial layers of the dermis are almost free from growth. The boundaries between deep fascia and subcutaneous tissue, and between the latter and the dermis have been obliterated by the growth; but the section clearly shows almost complete absence of growth towards the surface of the dermis, and a progressively increasing cancerous infiltration as the deep fascia is approached.

Slide 2.—A similar section opposite the first costal cartilage.

The epidermis and papillae have undergone atrophy. There are two layers almost free from growth, the superficial part of the dermis, and a thin layer of subcutaneous fat. There is no growth on the deep aspect of the dermis, though growth is present in its deepest layers.

The deep fascia is densely infiltrated by fibroid cancer. The deeper five-sixths of the thickness of the dermis is infiltrated by growth partly lying interstitially, partly in the lymphatics. The appearances are exactly those seen in a rather advanced skin nodule.

Slide 3.—A vertical section of the skin and underlying tissues of the affected side at the level of the second costal cartilage, near the middle line.

Superficially the epithelium is thin, and the underlying papillae appear atrophied. On the other hand the dermis appears thickened, and its fibrillae look swollen and ill-defined.

Its superficial layers show round-celled infiltration here and there, but no cancerous growth. About the junction of the superficial and middle layers of the dermis a few groups of suspicious cells, apparently lying in lymphatics, are visible. Except for these and a few scattered cells, the whole of the dermis is free from growth, save that at some points its deep surface is partially invaded by cancer spreading up from below.

The whole of the tissues below the subcutaneous fat are represented by a dense mass of fibroid and alveolar cancer which has replaced and destroyed the deep fascia.

The subcutaneous fat, here a very thin layer, has for the most part been involved in and destroyed by the growth, but is in places unaffected.

Slide 4.—The tissues from pleura to skin in the fourth intercostal space on the affected side.

The epithelium and its papillae are atrophied. The skin is 3 mm. thick. The superficial layers of the dermis show round-celled infiltration. The dermis is thickened and swollen. At one place its whole thickness is free from growth down to and including the superficial layers of the subcutaneous tissue, except for three or four small groups of cancer-cells lying in the deeper layers of the dermis. At another point five-sixths of the thickness of the dermis is infiltrated, but even here there is no growth in the superficial sixth. Between these two extremes there are all gradations.

All the tissues deep to the skin show dense infiltration by cancer though here and there little islets of fat have escaped.

The Seat and Source of the Lymphatic Obstruction in Cancer "en Cuirasse."

From the evidence just brought forward it is almost certain that early cancerous pachydermia is accompanied by, and is due to, obstruction of the deep fascial lymphatic plexus by extensive cancerous permeation, or to actual destruction of the lymphatic vessels of the fascial plexus by the process of perilymphatic fibrosis described in Chapter IV.

CHAPTER IX.

NATURAL PROCESSES OF REPAIR IN CARCINOMA.

THE materials for a full consideration of the natural history of untreated cancer are at present wanting, and hence the present chapter must be a mere outline sketch. The subject could be studied from one point of view by careful and frequently repeated observations and measurements carried out on the superficial metastases, such as subcutaneous nodules. The scantiness of our present knowledge of the natural course of untreated cancer, makes it impossible to estimate the precise value of the new remedies for cancer which are continually being introduced.

The Spontaneous Cure of Breast Cancer.

The fact that an untreated cancer is almost inevitably fatal is sometimes regarded as a proof that the body is entirely destitute of defensive resources against the disease. This pessimistic view found perhaps its most eminent supporter in Velpeau, and appears to owe its vitality mainly to his influence. He says emphatically:* "Abandoned to the resources of nature, cancer never disappears. Those who believe or affirm the contrary are mistaken. Their assertions depend upon errors of diagnosis, or, at any rate, from their confounding tumours of different kinds under the title of cancer." Velpeau divides cases of apparent natural cure into two classes, (*a*) Fungating encephaloid cancers, with spontaneous sloughing of the growth, and perhaps partial cicatrization of the ulcer which remains. In these cases a portion of the growth almost invariably escapes destruction. (*b*) Atrophic scirrhus cancers which ulcerate, become depressed and contracted, pucker the surrounding skin, and finally

* Velpeau, "Diseases of the Breast."—Sydenham Soc. Trans., p. 447.

become covered by a scarlike pellicle. The scar, however, is found to rest upon a stony mass of scirrhus which has increased in size, instead of diminishing or disappearing. Or new growths will have formed either in the neighbourhood, or in organs more or less distant.

If, concludes Velpeau, therapeutical science were destined to remain as powerless as the constitution itself where cancer is present, we should have nothing left but despair from the moment that we recognised the existence of the disease.

We have it, therefore, on the authority of an observer of vast experience, that the natural cure of cancer never occurs. But even the largest personal experience is inadequate to prove such a negative. Since Velpeau's time several cases of spontaneous cure have been recorded, and the most convincing of these cases, that of Mr. Pearce Gould,* may here be briefly summarised.

The proof of cure is not absolute, for the patient is still living, and the old saying, "Call no man happy until he is dead," applies with especial force to an individual who has suffered from cancer.

The patient first noticed a small mass in the left breast in 1888. In May 1890 this was diagnosed as scirrhus mammae, and amputation of the breast was performed. The tumour was examined microscopically and pronounced "typical scirrhus cancer" by two competent observers. In July 1892 a mass in the axilla was cleared out. In February 1894 recurrent nodules about the scar and a mass above the right breast were removed by a third operation. In December 1894 several nodules made their appearance about the scar, and there was great dyspnœa. The patient was now advised to seek admission to the wards for inoperable cancer cases at the Middlesex Hospital. On January 17th, 1895, the date of her admission, she showed numerous nodules about both mammary cicatrices, enlarged hard glands in both axillae and in both supra-clavicular fossæ, and great dyspnœa and emaciation. A secondary nodule appeared later in the left femur, and spontaneous fracture occurred. The patient remained in the Hospital under constant observation, and her condition did not alter appreciably until November 6th, 1895, when she left by her own desire.

In March 1896 her condition was still practically unchanged, but on June 15th, 1896, she was again carefully examined, and the

* A. Pearce Gould, Trans. Clin. Soc. Lond., Vol. xxx., 1897, p. 205, and Vol. xxxii., 1899, p. 272. See also the case of Vulpian, "Gazette des Hôp." 1885.

following notes were made :—One minute nodule in the skin above the left scar. The right scar keloid, and thicker in the centre. No enlarged glands in either axilla or above either clavicle. No dyspnœa. Left thigh deformed but less painful. On November 27th, 1896, the case was shown at the Clinical Society. The patient walked with a limp owing to shortening of the left leg, but no nodules could be detected anywhere. A somewhat keloid condition of the right scar was noted.

On April 28th, 1899, the patient was again shown at the Clinical Society, and she had undergone a further improvement in health ; the lameness was as before, and the local condition of the breasts was as follows :—The scars over the chest are all soft and supple, and there is not the slightest indication of any growth either in the chest-wall, the glands of the axillæ or of the neck, the liver or the lungs.

During the patient's stay in the Middlesex Hospital the medicinal treatment was of the usual kind, and directed to the relief of pain, dyspnœa, etc. No special form of treatment was adopted.

At the present time (May 1906) Mr. Pearce Gould informs me that he has temporarily lost sight of this patient.

Atrophic Scirrhus.

The apparently complete disappearance of a cancer in the acme of its career of dissemination is, of course, one of the rarest events in medicine, but cases are not uncommon in which the struggle between the cancer and the individual is prolonged and doubtful. Such appears to be the true explanation of cases of atrophic scirrhus. In the most marked form of atrophic scirrhus a puckered scar, to which the skin may be attached, slowly forms in the breast. The whole breast becomes somewhat shrunken and the nipple indrawn, but no definite tumour makes its appearance.

The disease in this form is usually painless, and the patient's attention is attracted only by local puckering and adhesion of the skin. Two such cases have recently come under my observation at the Middlesex Hospital, one a patient in Dr. Essex Wynter's wards, admitted for reasons unconnected with the condition of the breast, the other in my out-patient clinic.

In such cases the patient may die of some other disease, or after many years' local malignant ulceration, or metastatic tumour-formation, may terminate the case.

In less extreme cases of atrophic scirrhus the primary focus, after attaining the dimensions of a definite tumour, subsequently shrinks and disappears, or leaves only a mass of dense fibrous tissue, in the central portion of which no trace of malignant epithelium can be found. Complete fibrosis of the primary growth does not necessarily or usually prevent dissemination, which, however, in these cases, is very slow, attacking rather the skin, subcutaneous tissue and bones, than the internal organs.

We have now to consider from the clinical standpoint certain phenomena of partial and local repair in breast cancer.

The Epitheliation of Cancerous Ulcers.

Mr. Pearce Gould * mentions three cases in which partial or complete cicatrization of carcinomatous ulcers of the breast was observed.

Case 1.—A man, aet. 86, with an advanced and ulcerated scirrhus of the right breast. Twenty years previously he had an epithelioma removed from the lower lip. Near the deepest part of the mammary ulcer a small islet of cutaneous epithelium made its appearance, and commenced to spread over the floor of the ulcer.

Case 2.—A woman with advanced malignant disease of the left breast. No operation had been performed. There was a large malignant ulcer extending to the left axilla, upon whose surface several islets of growing epithelium made their appearance. Their growth seems to have continued up to within a few weeks of her death.

Case 3.—A woman with advanced malignant disease of the right breast. No operation had been performed, but the growth had entirely destroyed the breast. On admission, in addition to numerous secondary deposits in the opposite mamma, in the skin, muscles, and bones of the chest, and in the liver, she had a large ulcer occupying the position of the right mamma, with the edge showing a white line. Gradually the epithelium advanced over the ulcer until it was entirely healed. Within a month of complete healing the patient died with deposits in the lungs and liver. A section of the floor of the healed ulcer, made by Dr. Campbell Thomson, showed normal cutaneous epithelium, overlying fibrous tissue in which are embedded characteristic remains of the original scirrhus growth.

* A Clinical Lecture on "Cases Illustrating Repair in Cancer of the Breast," *The Clinical Journal*, May 9th, 1900.

In a case recorded by Mr. Nunn* cicatrisation of the ulcer was preceded by sloughing of the growth *en masse*. The lower half of a cancer of the breast sloughed away, leaving a surface which presently assumed the appearance of a healthy granulating and cicatrising sore. In this case it seems evident that the sloughing resulted from invasion of the growth by micro-organisms and not from any hostile reaction of the normal tissues.

As a rule the cicatrisation of cancerous ulcers does not seem in any way to delay the fatal event of the case. Nevertheless, such cases prove, in Mr. Pearce Gould's words, that "we are justified in speaking of repair in cancer, even in its advanced stages," and this conclusion "justifies—nay, compels—a belief in the possibility of the cure of cancer, and gives us an indication of the direction in which a cure is to be sought."†

The Disappearance of Subcutaneous Nodules.

The disappearance of malignant nodules in the subcutaneous tissues has been repeatedly observed by various surgeons. Short of total disappearance, such nodules may shrink up, and may be found on section to consist entirely of fibrous tissue. I recently had to examine a subcutaneous nodule from the mammary region, one of many which were present, removed for purposes of diagnosis. It proved to consist entirely of fibrous tissue, but nevertheless from the history of the case and the microscopic appearances, I was confident that the nodules were in origin carcinomatous. No special treatment had been applied.

Various agents, such as the injection of glacial acetic acid (Moore), or the application of X-rays, will cause shrinkage and disappearance of subcutaneous nodules. After the lapse of some weeks or months a nodule apparently destroyed by glacial acetic acid may reappear.

The Union of Cancerous Fractures.

Union of cancerous fractures is not a very rare, though doubtless an exceptional, event. Several cases occur in the

* Nunn, "Cancer," p. 24. Glaisher, 1899.

† Pearce Gould, loc. cit.

Records of the Middlesex Hospital for the last thirty years. In one case fractures of both humeri, of the left clavicle and the left femur had united, while ununited fractures of three metacarpal bones were present. In such cases, as in the shrinkage of subcutaneous nodules, fibrosis of the secondary deposit doubtless plays the chief part.

Shrinkage of Spinal Metastases.

Prof. Osler * has recorded two cases of spontaneous relief from symptoms indicating pressure upon the spinal cord by metastases in the spinal column. The second of these cases may here be quoted :—

> The primary operation was in February, 1898. In August, 1899, she began to have the usual nerve-root pain, and in November she had a severe attack of herpes on the left side. After a winter of great suffering she became completely paraplegic, and for weeks was desperately ill. In July she was moved to the country, and she began to get better. The paraplegia disappeared, and she regained control of the bladder and bowels. She walked stiffly, with the back bowed ; but from this time on until her death in January, 1903, she had no further paralysis. She took about 3 gr. of morphine daily. When the paraplegia existed there were nodules about the scar, and the glands in the neck were enlarged, but they progressively diminished in size. One skin nodule ulcerated and never entirely healed, but gave her no trouble. Four months before her death she had anorexia with vomiting, and stiffness of the right arm, but there was no recurrence of the paraplegia, nor did the secondary tumours increase in size. The patient lived for between three and four years after the onset of a paraplegia, due, there can be no question, I think, to pressure of a secondary mass in the spine.

The Shrinkage of Cancerous Lymphatic Glands.

This important question has never been properly studied, but there is reason to believe that the successful cancerous invasion of a lymphatic gland is often preceded by fruitless attempts at invasion, and that lymphatic glands possess considerable power of destroying cancerous epithelium (see p. 52 and p. 135, etc.) I have examined sections of enlarged glands, situated near a primary cancerous growth, which consisted

* Osler, "The Medical Aspects of Breast-Cancer."—*Brit. Med. Journ.*, Jan. 6th, 1906.

almost entirely of fibrous tissue. And in a case of breast cancer in a late stage I have observed an intermittent enlargement of the axillary glands on the side opposite to the growth. On some occasions these glands were as large as almonds, while on other intervening occasions they were quite impalpable.

The Concomitance of Growth and Repair in Carcinoma.

A most important deduction may be drawn from the investigations described in Chapter IV, namely, that certain processes of repair—which, in exceptional cases, may become clinically manifest by the disappearance of massive secondary deposits—are a normal part of the cancer process. The body of a cancer patient is not a passive culture-medium for carcinomatous epithelium, but a battle-ground where a fierce struggle for existence is waged between the normal and the cancerous tissues. The opposing forces are often closely matched and may be balanced almost to a nicety, as in the cases of atrophic scirrhus, but almost always the ultimate triumph of the carcinoma cells is ensured by their unlimited power of proliferation and by certain defects in the defensive process. There can be no doubt, however, that in the average case of cancer, before the disease attains its final victory, myriads of cancer cells are destroyed. This is not a mere picturesque statement, but a proved fact, whose importance needs no emphasis. The acceptance of the view that *in nearly all cases the local destruction of cancerous foci is a normal event of the cancer process*, is forced upon anyone who appreciates the facts of perilymphatic fibrosis (see p. 85) —the destruction of permeated lymphatics by an inflammatory reaction.

The Chemical Evidence for Defensive Processes.

The evidence for repair derived from clinical observation is lacking in precision, in that it cannot tell us how that repair takes place. The precise nature of the processes involved may be investigated in two directions, chemical, and microscopical. The former method is still in its infancy, and awaits the further unravelling of the complexities of proteid chemistry which has been begun by Gowland Hopkins and Mann in this country, and by Emil Fischer in Germany.

Attempts have been made, among others, by Colwell, Douglas and Lazarus-Barlow at the Middlesex Hospital, to apply the empirical precipitin methods of blood examination to the study of carcinoma, and using an animal as a living test-tube to detect something specific in the chemistry of cancer, and to find whether there is a chemical defensive mechanism against it. Time alone can show what measure of success awaits efforts in this direction. They represent a vast advance upon the crude attempts formerly in vogue to detect the essential nature of tumours from percentage analysis of the chemical elements which enter into their composition. At present the weight of evidence rather tends to show that there is nothing specific in the chemical nature of the carcinoma cell as compared with a normal epithelial cell. And no one has yet discovered a specific staining reaction for carcinomatous epithelium. I have shown in Chapter IV that the "healthy" cancer-cell, as seen at the microscopic growing edge is, at any rate, not sufficiently alien in composition to the normal tissues to excite any inflammatory reaction, or visible local reaction of any kind.

In the close affinity which appears to exist between a cancer-cell and the normal epithelial cell lies probably the chief difficulty of the cancer problem, since the discovery of a selective poison for cancerous epithelium is thereby rendered extremely unlikely.

The Microscopic Evidence for Reparative Processes.

Turning now to the microscopic evidence that the bodily economy possesses a defensive mechanism against cancer, the main emergent facts are, first, that the defensive reaction is a local, not a constitutional one, and secondly, that, such as it is, it resides mainly in the processes of inflammation and fibrous tissue formation. These conclusions may, I think, fairly be drawn from the evidence adduced in Chapters I and IV.

Local Nature of the Defensive Processes against Carcinoma.

In considering the clinical evidence for repair in carcinoma, it became obvious that the disappearance of a cancerous

nodule, the skinning over of an ulcerated primary growth, the repair of a cancerous fracture, afford only the slightest ground for hoping that the advance of the disease has been arrested. At the very time when local repair is taking place the disease is making headway in other directions. The study of the microscopic growing edge of a cancer enforces the same lesson. Lines of actively proliferating "healthy" cancer-cells are seen pushing their way unchecked along the lymphatic plexuses, while simultaneously, nearer the primary growth, the destruction of the permeated lymphatics may be seen in progress in all its stages.

It would thus appear, so far as the evidence goes, that the reparative processes which occur in cancer do not indicate immunisation of the organism against the invading epithelium by the development of an antitoxic substance in the fluids of the body, for such a substance, if present, might be expected to act equally upon all the carcinoma cells present in the body.

Inflammation the Main Factor in the Reparative Process.

The various stages in the destruction of a permeated lymphatic by "perilymphatic fibrosis" have already been traced in Chapter IV. (see also Fig. 12, p. 86). The permeated lymphatic acts as a foreign body, and is enveloped first by round cells, and afterwards by fibrous tissue. The enclosed cylinder of cancer-cells is strangled and killed by the contracting fibrous tissue, and finally removed by phagocytosis.

What is the cause of this inflammatory reaction? It has already been shown that it is absent in the earliest stage of permeation, the stage seen at the extreme "microscopic growing edge." It therefore cannot be ascribed to the irritative effect of the secretory or excretory products of the cancer-cell as such. As has been stated in Chapter IV., perilymphatic fibrosis is excited only by those cancer-cells which, as the result of the pressure produced by their own proliferation within the walls of the enclosing lymphatic, have become so far devitalised as to act like foreign material in reference to the other tissues of the body.* The active

* Orth has independently reached similar conclusions. "Ueber Heilungsvorgänge in Epitheliomen." Zeitschrift für Krebsforschung, Vol. i., No. 5, 1904.

"healthy" cancer-cell seen at the extreme microscopic growing edge, well nourished and not exposed to pressure, excites in cancerous patients no leucocytic hostility, but is accepted as a normal denizen of the body, and hence the ultimate failure of natural attempts at repair in nearly every case of carcinoma.

The foregoing facts supply some sort of basis for the hope that the cure of cancer might be found in the discovery of means for exalting the activity and increasing the number of the leucocytes. Efforts have indeed already been made in this direction, but it is much to be feared that methods of increasing leucocytic activity will be futile until some way of simultaneously poisoning the cancer-cell is discovered. Otherwise, only the massive macroscopic secondary growths will be affected, in which the processes which lead to the death of the cancer-cell are sufficiently advanced to give the leucocytes their opportunity.

In any case it is evidently important to avoid, in the treatment of cancer, anything which is likely to impair the vigour of the patient's inflammatory reaction. For instance, it appears to me probable that at present the tendency is towards over-dosage in the application of X-rays to malignant growths. It is known that X-rays possess the power of killing leucocytes, and doubtless also, in smaller doses, of decreasing their activity. May not the *persistent* application of X-rays ultimately favour the growth of a cancer by checking and interfering with the inflammatory process?

The Chemiotactic Influence of Cancer-cells upon the Leucocytes.

According to my observations the living cancer-cell in its most active state, not degenerate from pressure or any other cause, exerts no attractive influence upon the leucocytes. On the other hand, a cancer-cell which is undergoing degeneration as the result of pressure, either itself exerts a strong positive chemiotactic influence upon the leucocytes, or sets up in the surrounding non-cancerous tissues changes which attract the leucocytes to those tissues. The leucocytosis which occurs in the late stages of permeation is not confined to the peri-lymphatic tissues. Frequently, also, the blood vessels in the neighbourhood are crowded with white corpuscles.

The absence of round-celled infiltration at the "microscopic growing edge" is strong evidence against the ingenious theory that conjugation of a leucocyte with an epithelial cell is the essential event of the cancer process. The observations upon which this theory is based probably represent stages in the phagocytosis of the cancer-cell.

The Natural Defensive Mechanism as an Aid to Operative Treatment.

In connexion with the operative treatment of cancer, it is of the first importance to obtain a definite answer to the question: Can the surgeon hope for, or expect, any assistance from natural processes in his efforts to eradicate the disease? If this question had to be answered in the negative,—if a solitary living cancer-cell left by the operation must inevitably reproduce the tumour, then the outlook would be black indeed for any except the earliest cases. But a considerable body of evidence has been adduced to show that Nature possesses some means at any rate, however imperfect, of defence and repair against the invading epithelium. It is, therefore, legitimate to operate even in cases where the ideal of complete extirpation, though not abandoned, seems unlikely to be attained. By removing the bulk of the disease and thus sufficiently reducing the dose of the poison, the surgeon may possibly, in some cases, decide the doubtful struggle against the neoplasm and in favour of the patient, although the absence of inflammatory reaction at the "microscopic growing edge," the portion most likely to be left behind by the operation, indicates that such a favourable issue is likely to be an exceptional event. Nothing could be more dangerous than to *rely* on the natural tendency to cure in cancer, or to use it as an excuse for slipshod operating. But it does go far to justify attempted removal of the growth in cases verging on the border line of operability.

Operations for Recurrence.

In some cases of breast cancer a gradual diminution in the virulence of the cancerous process, or perhaps, rather, a gradual exaltation of the patient's powers of resistance, seems

traceable. In Mr. Pearce Gould's celebrated case of spontaneous cure it is not improbable that the three operations which were performed gave time for the development and success of the natural powers of resistance, and that but for these operations the patient would have succumbed to the disease. Mr. Clement Lucas,* by repeated operation, prolonged life in one of his cases for upwards of eight years. The only contra-indications to immediate operation for recurrence are those which would equally bar a primary operation.

Fallacies in the Therapeutics of Cancer.

According to the permeation view of dissemination *the progress of a cancer is normally accompanied by retrogressive or curative processes.* It is not surprising, therefore, that occasionally visible nodules, or even the primary growth itself, should undergo complete fibrosis in the same way as does a permeated lymphatic, nor that in such cases of partial cure the appearance of fresh metastases elsewhere soon shatters the false hopes which have been raised.

A happy ignorance of this aspect of the natural history of carcinoma has not infrequently enabled the discoverer of a medicinal cure for cancer to maintain a sincere faith in his remedy for some considerable time. The natural regressive processes, which in untreated cases usually pass unobserved, are ascribed to the action of the remedy.

* Clement Lucas, *Brit. Med. Journ.*, Sept. 1st, 1888.

CHAPTER X

ANATOMY OF THE BREAST AND AXILLARY GLANDS.

It is unnecessary to transcribe the descriptions of the anatomy of the breast found in anatomical text-books, but certain points require special mention.

The Limits of the Mamma.

By means of his nitric acid method, Stiles * has shown that the breast is a much more extensive organ than was formerly thought, and it is important to bear this fact in mind, although the operation for breast cancer is not merely an "amputation of the breast." The breast may be divided into quadrants by vertical and horizontal lines, and further sub-divided by two oblique diameters lying midway between those bounding the quadrants. The vertical diameter extends from the lower border of the second rib to the sixth costal cartilage at the angle where it begins to sweep upwards towards the sternum. The horizontal diameter extends from a little within the edge of the sternum, opposite the fourth rib, to the fifth rib opposite the mid-axillary line. One oblique diameter extends from the upper border of the third costal cartilage, a little outside the sternum, downwards and outwards to the seventh rib a little in front of the mid-axillary line, the other oblique diameter passes from the third rib a little beyond the anterior axillary fold downwards and inwards to the sixth costal cartilage midway between its angle and its sternal end. As regards the lower end of this diameter it is important to notice that it is situated only about an inch from the "dangerous area"—the area of epigastric invasion.

* Stiles, *Edin. Med. Journ.*, July, 1892.

The Relations of the Deep Surface of the Breast to the Underlying Muscles.

The relations of the breast to the muscles which underlie it have been worked out by Stiles. The inner hemisphere rests almost entirely on the pectoralis major; at its lowest part it slightly overlies the aponeurosis of the external oblique of the abdomen, and the origin of the rectus muscle. The upper half of the upper and outer quadrant of the breast rests on the greater pectoral, and, to a slight extent, on the serratus magnus, upon which, and under cover of the pectoralis major, it extends upwards into the axilla as high as the third rib (axillary tail of the mamma). The lower half of the upper quadrant, and the upper half of the lower quadrant rest almost entirely on the serratus magnus, with the exception of a small area adjacent to the nipple, which overlies the pectoralis major. The lower half of the lower quadrant touches the digitations of the serratus and external oblique which arise from the fifth and sixth ribs, and the part near the nipple lies on the pectoralis major. Thus about one-third of the mamma lies inferior and external to the axillary border of the pectoralis major. Of this portion the upper half overlies the lower part of the inner wall of the axilla, and is separated from its contents by the axillary fascia, here so fatty that the lymphatic glands lying embedded in it appear to be in direct contact with the breast.

The Anatomy of the Axillary Glands.

All attempts to give an absolutely precise description of the axillary glands are defeated by the great variations in number and arrangement which they present. Cunningham describes them in four groups:—

(*a*.) A chain of six or more glands lying close to the axillary vessels, which extends from the lower border of the pectoralis major and receives the lymphatic vessels ascending from the limb. The highest of these glands (sometimes called the subclavian glands) lie in the space of Mohrenheim under cover of the clavicular part of the pectoralis major, behind the costo-coracoid membrane. These

glands, situated high up at the apex of the axilla, have a special importance for two reasons, firstly because they are sometimes found cancerous even when the pectoral glands have escaped (Stiles), and secondly because, as Mr. Pearce Gould has pointed out, they are very likely, owing to their sheltered position, to escape removal during the operation unless special attention is directed to them. It is almost impossible to reach them unless the greater part of the pectoralis major is removed. Mr. C. B. Lockwood * has recently re-directed attention to these so-called subclavian glands, which, as Grossmann has pointed out, in 10 per cent. of all cases receive a tributary from the breast which reaches them directly by piercing the pectoralis major muscle. This lymphatic channel is depicted in Poirier's work on lymphatic anatomy.†

(*b.*) A group of pectoral glands placed along the lower border of the pectoralis minor and on the inner wall of the thorax in the angle between the pectoral muscles and the serratus magnus, which are joined by lymphatics from the mammary gland and from the front of the chest.

(*c.*) A group of subscapular glands situated along the lower border of the subscapularis muscle on the posterior wall of the axilla, into which the lymphatics of the back pour their contents. This set of glands is not as a rule affected in breast-cancer, but may be cancerous in very advanced cases.

(*d.*) Leaf has described a "central" set of glands sometimes lying superficial to the axillary fascia, sometimes just deep to it.

(*e.*) The uppermost glands of the chain which sometimes extends from the bicipital gland to the axilla may be affected in breast-cancer (Lockwood).

* C. B. Lockwood, "An Address on Carcinoma of the Breast."—*Brit. Med. Journ.*, Jan. 27th, 1906.

† A translation has recently been made by Mr. C. H. Leaf, who has done much to revive interest in the important but neglected subject of lymphatic anatomy.

Besides the larger lymphatic glands, obvious to the naked eye on dissection, the axillary lymphatics present in their course innumerable tiny interrupting nodules of lymphoid tissue, each of which is a perfect lymphatic gland in miniature.*

Unless the whole of the axillary fat is removed, some of these lymphoid nodules are certain to be left behind. Many of these minute glands, as Stiles has shown, may be found undergoing fatty degeneration, or on the other hand they may be found during pregnancy or lactation in a high degree of development. The lymphatic gland system of the axilla is, in fact, a highly mobile mechanism, which adapts itself from time to time to the demands made upon it. As Stiles points out, it is even possible that fat lobules may, if the need should arise, develop into lymphoid nodules.

* Harold Stiles, "Contributions to the Surgical Anatomy of the Breast."—*Edin. Med. Journ.*, 1892.

CHAPTER XI.

THE HISTORY AND RESULTS OF OPERATIVE METHODS FOR BREAST-CANCER.

MANY of the principles which underlie the present operative methods of dealing with breast-cancer were laid down by Mr. Charles Moore, then Surgeon to the Middlesex Hospital, in a paper on inadequate operations for cancer,* which was published in 1867. Moore must therefore be regarded as the father of modern breast surgery as applied to cancer. He showed that recurrence after operation is due, not to an organic or constitutional taint, but to incomplete removal of the primary growth and its surrounding satellite nodules. He insisted that the growth, with all its ramifications, must be removed in one piece, and must not be cut into or seen during the operation. In order to carry out this principle he enunciated the necessity, in every case, of removing the whole breast, along with unsound adjoining structures—skin, lymphatics, fat, pectoral muscle, and axillary glands. After freely removing the unhealthy skin, he undermined the skin-flaps, so as to reach the circumference of the breast, which he then detached from its circumference towards its centre. He did not, however, state precisely how he would define the "unsound adjoining structures" requiring removal, nor did he give an exact description of his operative method.

Moore's teaching, though it became an accepted tradition of the Middlesex Hospital, met with strong opposition in this country, perhaps because of the immediate danger—in the pre-antiseptic period of surgery—of the operation which he advocated.

* "On the Influence of Inadequate Operations on the Theory of Cancer." Trans. of the Royal Med.-Chir. Soc., Vol. l., 1867, p. 245.

Towards the end of the "sixties," according to Professor Cheyne,* Lord Lister began to practise a very free operation, which included in most cases the free removal of skin and ablation of the pectoral fascia and axillary glands. The late Sir Mitchell Banks † in 1882 advised the removal of the whole breast, of the skin over it, of the pectoral fascia, of the fibres of this muscle (if at all suspicious), and the routine removal of the axillary glands.

So late as 1887, when Banks read a paper at the Harveian Society advocating the removal of the axillary glands in every case of breast-cancer, the President of the Society, Mr. Edmund Owen, was the only speaker who supported the reader of the paper. The change of English opinion on this subject is largely owing to the pathological work of Stiles, and to the striking contributions in recent years of two distinguished American surgeons, Gross and Halsted, whose work was independent of that of Moore.

As the result of careful and extended statistical enquiry Gross (1888) insisted on the necessity of removing the axillary glands in every case of breast cancer. He pointed out that isolated lobules of breast tissue were frequently to be found at some distance from the main body of the gland. He excised the whole of the skin over the prominent portion of the mamma. But though his operation led to somewhat improved results, it had the defect—in my opinion a capital one,—that the area of deep fascia excised was no larger than the area of skin removed. If nodules were seen in the pectoral muscle he excised large portions of it. The breast was ablated before the axillary contents were attacked. The axilla was reached by an incision passing up into it about three-quarters of an inch below the lower border of the great pectoral muscle, thus avoiding the objectionable scar along the anterior margin of the axilla which is still so often seen.

Mr. Jacobson ‡ in 1891, advocated the clean removal of the sternal portion of the pectoralis major, if the appearances in any way indicated its involvement.

* "The Treatment of Cancer of the Breast by Operation."—The *Lancet* March 12th, 1904.

† *Brit. Med. Journ.*, 1882, Vol. ii., p. 1138.

‡ "The Operations of Surgery," 2nd edition, 1891, p. 576.

Stiles (1893) pointed out that Gross's method removes an unnecessary amount of skin, that it does not ensure removal of the outlying breast lobules, nor take away enough of the circum-mammary fat He advocated an elliptical skin incision, measuring four inches in its short diameter, and prolonged to the axilla along the lower border of the pectoral. A further V-shaped portion of skin was removed if the growth was an eccentric one. The lower and outer flap was then to be dissected off the breast, keeping as close to the skin as was consistent with the maintenance of its vitality. The dissection was to be carried as low as the seventh rib in the mid-axillary line. The upper and inner flap was reflected inwards beyond the edge of the sternum, and upwards almost as high as the clavicle. The extreme outlying portions of the breast thus being rendered accessible, the organ with the fascia underlying it and covering the pectoralis major, serratus magnus, and the uppermost digitations of the external oblique, was to be lifted from the thoracic wall. The axillary tissues were then removed in continuity with it. In Stiles's opinion, complete removal of the breast is necessary in every case, not so much on account of diffuse pre-cancerous changes throughout the breast such as Heidenhain described, but rather to ensure ablation of the cancerous lymphatics which are so frequently found throughout the organ. The general recognition of Stiles's work in England is largely due to the advocacy of Prof. Watson Cheyne, whose first paper on the subject was published in 1892.

Professor Halsted* (1894), by the publication of a full and precise description of his operation, gave a great impulse to the movement in favour of more radical treatment. He was the first to advocate removal of the sternal half of the great pectoral muscle in every case, and to him belongs the credit of converting the profession to the necessity of this step. He advised division of its clavicular half, and of the pectoralis minor, so as to obtain perfect access to the axilla. He insisted on removal of the breast and axillary tissues in one piece. He removed the whole of the skin over the breast, and left the wound to heal by granulation. In this respect his operation appears unnecessarily severe. On

* "Annals of Surgery," Nov. 1894.

the other hand he did not undermine the flaps so as to remove the deep fascia and outlying mammary lobules, and here present knowledge shows that his operation is seriously inadequate. Professor Halsted's work has made a deep impression on English opinion, so that any radical operation on breast-cancer which includes removal of the great pectoral is often erroneously described as a "Halsted's operation." Halsted in 1894 also advocated routine removal of the supraclavicular glands. Though he has abandoned this extreme position he still thinks this step is necessary in many, perhaps in most, cases of breast-cancer.*

The Comparative Results of the Different Methods of Operation.

It would be tedious and unprofitable to embark on the sea of statistics relating to operative results in breast-cancer. It is hopeless to attempt the combination or comparison of figures gathered from different sources. There can, however, be no doubt that the more recent methods of operation have greatly diminished the risk of recurrence. Perhaps the best evidence on this point is to be derived from the homogeneous statistics of a single large hospital, or from the personal experience and opinions of surgeons who have been in busy practice for a long period. In opening the discussion on a paper which I had the honour of reading before the Glasgow Medico-Chirurgical Society† in November, 1905, Sir Hector Cameron gave it as his opinion that the more recent methods of operation have, as a matter of fact, led to a marked improvement in results. This opinion is borne out by Campiche and Lazarus-Barlow from a study of the records of the Middlesex Hospital.‡ The result of their enquiries is summarised in Table VII.

* See a valuable paper on "Breast-Cancer," by Prof. Rodman, of Philadelphia.—*Brit. Med. Journ.*, October 1st, 1904.

† "On the Mode of Spread of Breast-Cancer in Relation to its Operative Treatment."—*The Glasgow Medical Journal*, December, 1905.

‡ Campiche and Lazarus-Barlow, "Malignant Disease of the Breast, a Statistical Study from the Records of the Middlesex Hospital."—Archives of the Middlesex Hospital, Vol. v., 1905.

TABLE VII.

Compiled from Campiche and Lazarus-Barlow, showing the comparative results of various methods of operation on Breast-Cancer practised at the Middlesex Hospital at various periods.

Nature of Operation.	Number of cases.	Percentage of cases presenting themselves with recurrence.	Average period intervening between operation and recurrence.	Average duration of life after operation *in cases returning with recurrence.*
Partial or complete amputation of the breast alone (1858—1875)...	200	54·5	22 months.	34 months.
Amputation of the breast and removal of the axillary glands (1875—1895)	230	39	10·5 „	29 „
Amputation of the breast and clearing of the axilla with removal of the pectoral fascia, pectoral muscle, &c. (from 1894) Operation mortality 1·5 per cent.	275	Upwards of 13·8	9·9 „	26 „

The salient feature of Table VII. is the large and progressive diminution in the percentage of cases presenting themselves at the Hospital with recurrence. This diminution cannot be ascribed to any other cause than improved methods of operation.

At first sight modern methods, as compared with older methods would appear from Table VII. to give a smaller average period of freedom from recurrence, and a diminished expectation of life. Such a conclusion is fortunately quite erroneous as applied to the whole number of cases; *it is only true as applied to the continually decreasing percentage of cases of recurrence.*

When the ideal method of operating on breast-cancer is attained, recurrence will only take place in those cases where visceral metastases, still clinically unrecognisable, are present at the time of operation. The period of freedom from recurrence, and the duration of life after operation in cases where recurrence takes place, will then be still further reduced. It is no argument against more recent methods of operation that, when they fail, the failure soon shows itself. The essential question is not "How quickly does recurrence take

place?" but "How often?" and the answer is emphatically favourable to the more radical methods of operation. Moreover, as Campiche and Lazarus-Barlow point out, cases that would formerly have been regarded as inoperable are now dealt with by the surgeon, a fact which must react prejudicially against the statistics of modern methods. The improvement they have wrought is greater than actually appears.

CHAPTER XII.

THE PRINCIPLES OF THE OPERATION FOR BREAST-CANCER.

The Area of Operation to be Concentric with the Growth.

If breast-cancer spreads by centrifugal permeation with approximate equality in all directions, but with a tendency to keep in certain planes pre-determined by the arrangement of the lymphatic vessels, there is one great principle to be observed in its operative treatment—a principle which has never hitherto been fully carried out. It is essential that (with regard to the plane of spread) the primary growth shall always be the central point of the mass of tissue which is cut out in order to remove the cancer. This principle is probably applicable, not only to the operative treatment of breast-cancer, but to that of carcinoma in all its forms, subject only to the practical difficulties frequently involved.

Aim of the Operation.

It is generally stated that the aim of the operation for breast-cancer is the removal in one mass of the whole breast with its outlying lobules, of the skin overlying the prominent part of breast, of the pectoral fascia and the pectoral muscle, of the lymphatics which run from the breast to the axilla, and of the axillary glands. The operation is frequently described as an "amputation of the breast," a most inadequate and misleading description, for owing to the fact that the lymph-vascular system of the body is a unity—a single vast anastomotic network of fine channels—the progress of permeation is not confined within the breast, nor is it arrested either by the limits of the pectoral fascia, or, indeed, by any anatomical boundaries whatsoever. While, therefore, complete removal of the breast is essential in every case on acount of possible precancerous changes, and of the readiness with which

permeation extends, widely or universally, through the especially rich network of mammary lymphatics, it is a necessary incident and not the sole object of the operation for breast cancer.

Similarly, with regard to the removal of the pectoral fascia, the lymphatic plexus lying on it is simply a part of the deep fascial lymphatic plexus, and unless the growth is an early one beginning in the centre of the breast, the circular permeated area of fasica may have overlapped the artificial boundaries of the pectoral fascia in one direction or another, and will at those points be left untouched by any operation which aims merely at the removal of the pectoral fascia. It is impossible therefore to define the limits of the operation by hard and fast anatomical landmarks. Its limits will vary according to the situation of the growth in the breast.

Stated in the most general terms possible the object of the operation should be *the removal intact of the permeated area of the lymph-vascular system which surrounds the primary growth, and of the lymphatic glands which may have been embolically invaded along the trunk lymphatics of the area concerned.*

How are the limits of this permeated area to be defined? It is impossible to see it with the naked eye, the operator can therefore only aim at keeping a safe distance beyond it. Of course the area of centrifugal spread in the deep fascia is not a mathematical circle, any more than is the area of spread of an ordinary case of erysipelas. Slight variations in the local conditions, whose nature is not yet understood, may lead to increased spread in one direction, to diminished spread in another. If one or two subcutaneous nodules are present on one side of the primary growth, the skin and deep fascia on that side should be removed more widely than in the opposite direction. But in the usual absence of evidence to the contrary the only safe assumption is that the cancer has spread equally in all directions. The area of spread is circular, not spherical, because permeation tends by preference to keep in one plane, that of the fascial lymphatic plexus. But later on permeation spreads into the small muscular and cutaneous tributaries which drain vertically into the fascial plexus, and so invades the adjoining layers to a depth which

reaches its maximum opposite the centre of the primary growth. Thus a breast cancer, with its invisible microscopic extensions, forms a mass shaped somewhat like a biconvex lens. The thin circumference of the lens, situated often far beyond the limits of the breast, is formed by the cancer-filled lymphatics of the fascial lymphatic plexus, and lies, as a rule, exclusively in the plane of this plexus. As one approaches the centre of the lens, which corresponds to the primary growth, the adjoining layers—the subjacent muscle on the one hand, and the subcutaneous fat and skin on the other—are invaded by cancer to a gradually increasing depth.

A detailed method for the removal of this lens-shaped mass of tissue, to the outer margin of which the fat and glands of the axilla must of course be left attached, will be described in the succeeding chaper.

The Planning of the Skin Incision.

Apart from questions of pathological principle there are certain points in connection with the planning of the skin incision which are important with reference to the closure of the wound, the comfort of the patient, and the subsequent usefulness of the arm.

The scar left by the operation is frequently a straight line running from the lower edge of the insertion of the great pectoral, along the anterior fold of the axilla, to a point somewhere near the ensiform cartilage. A case illustrating the disadvantages of such a scar came under my observation some time ago at the Samaritan Hospital.

Where it followed the anterior axillary fold the scar formed a sharp bridle-like prominence. The arm could not be raised more than thirty degrees from the side. and even this amount of abduction produced a pain passing along the line of the scar back to the left scapula, which the patient described as "like being screwed up in a vice." The patient asked for a further operation, not for any recurrence of the growth, but to relieve this pain on movement. Apart from its tendency to limit abduction, the present elliptical skin incision is likely to remove too little skin in the short axis, and an unnecessary amount of skin in the long axis of the ellipse.

The skin incision in breast-cancer has two objects: first, to isolate the presumably cancerous area of skin with a view to its removal, secondly, to afford the necessary access to the deeper parts. The incision surrounding the suspected skin area should be made entirely without reference to the subsequent suturing of the wound. The remaining part—the incision of access—should be purely linear, and its axillary portion should avoid the anterior edge of the axilla. Moreover, it should be made in such a way that the suture-line after the operation is complete shall not be a straight line. If the sutured incision is rectilinear, the skin tension must be almost exclusively in a direction at right angles to its length, whereas when the line of sutures is curved, or sinuous, or tri-radiate, the pull of the stitches acts in various directions, and the surrounding skin will be dragged in from all points of the compass, and will more easily cover the raw area.

During the contraction of the scar the disadvantages of the straight suture-line are as manifest as at the time of operation. It is evident that a scar situated in the line of the lower border of the great pectoral muscle, lying in a situation where a reserve of loose skin is requisite for free abduction, will, as it contracts, have a special tendency to bind the arm to the side. The full range of movement of the arm is only regained when the scar becomes mobile upon the bony thorax. Adhesion of the scar to the thorax, not removal of muscle, however free, is the chief obstacle to abduction of the arm.

And if the scar be a straight one, lying along the lower border of the pectoral, the pull of the arm in abduction is directly in the line along which the scar is adherent to the chest, and is opposed by the whole length of the line of adhesion. Under such conditions there is evidently little prospect of the scar becoming mobile, for the force tending to produce mobility meets with a maximum of resistance. If, however, the scar, or a portion of it, lies at right angles to the line of skin tension during abduction of the arm, it can offer but a weak resistance to the drag of the arm—the resistance of its breadth instead of its length—and the prospects of a mobile scar are much improved. Often, too, such

a scar will stretch considerably, so that, instead of being linear, it becomes where the tension is greatest, a broad band an inch or more in diameter, perhaps as thin as paper, but gliding smoothly over the subjacent costal cartilages (see

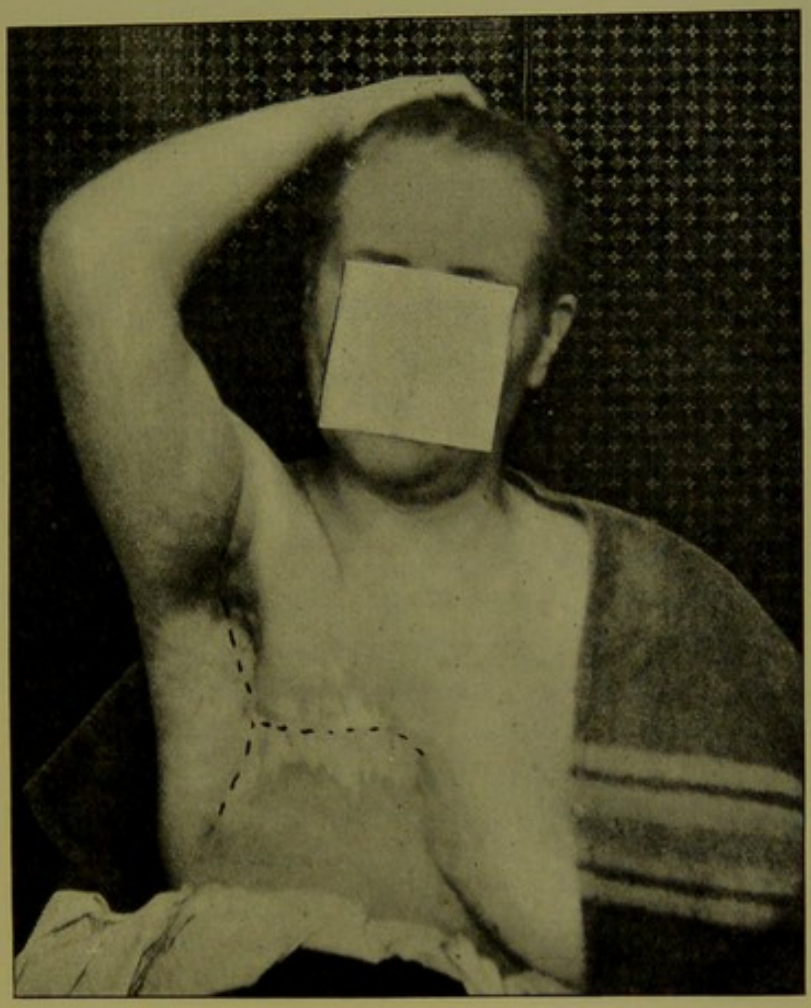


FIG. 42.

From a case of breast cancer operated upon by the author in 1903. To illustrate the advantages of a scar which lies at right angles to the line of skin-tension in abduction of the arm. The horizontal limb of the tri-radiate scar has stretched so as to form a broad band nearly an inch wide, freely movable over the costal cartilages. The vertical limb of the scar avoids the anterior edge of the axilla and lies in the axillary fornix. The arm is capable of abduction to the full degree.

Fig. 42). It is possible to employ an incision occupying the vault of the axilla and avoiding its anterior border, which without any loss of safety or convenience will obviate the disadvantages referred to (see next chapter); and, indeed.

some operators have for years past avoided incisions along the anterior border of the axillary outlet.

Removal of Skin.

The area of skin taken away in the operation should obviously be no larger than is necessary, and no healthy skin should be removed. It has already been shown that cancer does not spread in the plane of the skin, but, nevertheless, free removal of skin is necessary, owing to the vertical extension to the skin after a time, and over a smaller area, of the growth which is spreading in the deep fascia. The necessary conditions can usually be fulfilled by the removal of a circular area of skin four to five inches in diameter, with the growth at its centre.

The very extensive ablation of skin carried out by some surgeons is based upon erroneous ideas of the pathology of dissemination, and is not found practically to improve the results of the operation (see pp. 45 and 89).

If after the primary operation skin nodules appear in the neighbourhood of the scar, their significance varies according as they lie within the area from beneath which the deep fascia has been excised, or outside it. In the former case they are to be regarded merely as local deposits—"efflorescences"—whose roots have already been removed, though at the time of the operation they themselves were too small to be detected. Such nodules can, therefore, be excised with every prospect that recurrence in the neighbouring skin will not take place.

On the other hand, subcutaneous nodules appearing in an area where the deep fascia is still intact, indicate wide extension of the growth in the latter layer. If they extend more than three inches from the original primary growth the case must probably be regarded as hopeless, owing to the large area of fascia involved.

Removal of the Permeated Area of the Deep Fascia.

It is a fortunate circumstance that breast cancer spreads primarily in the parietes along the deep fascia and only secondarily involves the skin. For while removal of the skin has, in some hands, reached its furthest possible limits

without any corresponding improvement in results, it is possible to remove the deep fascia over a wider area than is yet the usual custom. The removal of a maximal circular area of deep fascia centred upon the primary growth, is a step absolutely essential to the completeness of the operation, except in very early cases. There is no technical difficulty involved, if only the skin-flaps are sufficiently undermined, a step whose importance has been long emphasized by Mr. Stiles and by my friend and teacher, Mr. Jacobson, and one which is very thoroughly carried out in the surgical practice of the Middlesex Hospital.

It is a significant fact that the operator, who has the best published operative results, lays stress on the removal of a wide area of deep fascia, following the lines laid down by Stiles. Prof. Cheyne says: ". . . . the skin incisions when made should not go straight down to the muscle. After the skin incisions have been mapped out, the skin and just sufficient fat to enable it to retain its vitality should be dissected up, and the muscular fibres should not be exposed till just below the clavicle above, beyond the middle line in front, over the origin of the abdominal muscles below, and over the edge of the latissimus behind." It will be found that, judged by the standard I have set up—i.e. the removal of a maximal area concentric with the growth—the area of deep fascia defined by Prof. Cheyne is very deficient in a downward direction, for the abdominal muscles arise well above the costal margin.

The following measurements show the distance from the nipple to various points on the thorax in two patients with non-pendulous mammae:—

	Patient No. 1.	Patient No. 2	Average.
Nipple to tip of ensiform cartilage	4 in.	5 in.	4½ in.
Nipple to nearest point of clavicle	5 in.	6½ in.	5¾ in.
Nipple to nearest point of middle line ...	3½ in.	4½ in.	4 in.
Nipple to nearest point of edge of latissimus dorsi	—	5 in.	5 in.

The distance from the nipple to the clavicle may be taken as the radius of the circle of deep fascia round the growth, which can, in practice, be removed without difficulty by undermining the skin flaps sufficiently and prolonging the incision somewhat in a downward direction:

If the growth starts under the nipple the deep fascia should accordingly be removed—

above ... ... up to the clavicle,
internally ... 1 to 2 inches beyond the middle line,
externally ... just beyond the anterior edge of the latissimus dorsi,
below ... ... *to a horizontal line running 2 inches below the tip of the ensiform cartilage.*

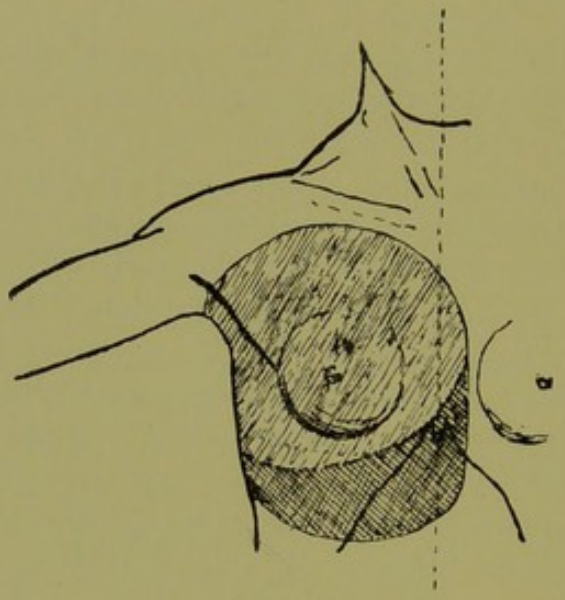


FIG. 43.

The lightly-shaded area represents the extent of deep fascia removed in the operation of excision of the breast, as at present usually performed.
The darkly-shaded area represents the additional extent of deep fascia which should, in future, be removed to ensure that the circle of invaded fascia shall be completely circumscribed and not intersected below.
The line surrounding the whole shaded area represents the extent to which the skin-flaps should be undermined for that purpose, assuming that the primary growth is situated beneath the nipple.

Coming now to growths situated near the margin of the breast, it is probable that the want of coincidence between the area of the present operation and the circle of infected fascia in these eccentric growths largely accounts for the bad prognosis associated with them.

The area of tissue removed should be concentric with the nipple only when the primary growth is situated just beneath

that structure. If a cancer is situated at the sternal margin of the breast it may be necessary to excise the deep fascia beneath the inner half of the opposite breast. If the growth is situated at the lower margin of the breast it may be requisite to excise the abdominal deep fascia far down towards the umbilicus. If the growth is situated in the axillary tail of the mamma, the deep fascia will require excision in the deltoid region, and far backwards over the surface of the latissimus dorsi. Unless these considerations are borne in mind the growing edge of fascial permeation will be left behind at one point or another.

Purely Visceral Recurrences sometimes due to Incomplete Operation.

It is frequently assumed that no defect in the operation can be held responsible for cases in which, after the operation for breast cancer, recurrence takes place only in the internal organs, while the parietes remain free from recognisable growth. Such a belief is not by any means invariably well-founded. It is a fact to be especially noted, that in a considerable proportion of cases of epigastric invasion, no clinically recognisable nodules can be felt over the abdominal wall even in the latest stages of the case. For example, the nodules seen over the rectus sheath in the frontispiece were not clinically palpable, although epigastric invasion had occurred. A recurrence in the abdominal viscera after operation may be due to the failure of the operator to remove a microscopically invaded portion of the epigastric deep fascia, even though no subcutaneous nodules of growth subsequently appear in the epigastric region to indicate the incompleteness of the operation.

The cancerous process smoulders like a slow-match in the lymphatics of the epigastric parietes, and perhaps in this region finally dies out altogether, having meantime penetrated to the peritoneum and given rise to an explosion of metastases within the abdominal cavity, where the conditions are so favourable to widespread dissemination and rapid multiplication of the cancerous epithelium.

The Excess of Abdominal Recurrences following Present Methods of Operation.

That the present methods of operation do, as a matter of fact, frequently leave microscopic permeated lymphatics in the deep fascia of the epigastric region, is rendered highly probable by a study of the relative frequency of abdominal and thoracic recurrences in Prof. Cheyne's series of cases. His precautions against invasion of the thorax cannot be made more thorough, and consequently, by his method recurrences in the thorax are reduced to a minimum. On the other hand his method does not reckon with the danger of direct abdominal invasion through the epigastric parietes. What is the consequence? That in his series of cases abdominal recurrence becomes relatively far more frequent than thoracic recurrence.

Thirteen of his first series of 61 cases died after operation with visceral metastases. These cases were—

Case 2. An abdominal swelling developed nine months after operation. Death 21 months after operation.

Case 3 showed nodules in the ribs, and there was a presumption of mediastinal growth.

Case 4.—Secondary cancer of intestine (*vide* "Lancet," 18th March, 1899).

Case 7.—Metastatic deposit in the lungs. Died in about 18 months.

Case 8.—Masses felt in the abdomen (? metastases in the ovary).

Case 10.—Cancer of pleura. Died 21 months after operation.

Case 17.—Deposit in lower part of spine. Died 21 months after operation.

Case 24.—Died from intestinal obstruction, with a tumour in the abdomen.

Case 33.—Pain in back. Probable recurrence in vertebræ.

Case 38.—Recurrence in abdomen. A subcutaneous nodule near edge of latissimus dorsi removed at a secondary operation.

Case 41.—Complaint of sacral pain after the operation. Probably spinal deposit was present at the time of the operation.

Case 56.—Became weaker and died in 3 months. Nodules could be felt in the abdomen, no doubt cancerous.

Case 60.—Recurrence in liver. Death 18 months after operation (*Lancet*, 18th March, 1899).

No necropsy appears to have been made in the majority of these cases. But it is noteworthy that only two (? three) of them died with symptoms of thoracic recurrence, while in seven cases the recurrence was clearly of an abdominal type. In two of the remaining three cases there was recurrence in the *abdominal* portion of the spine, while in the third there was deposit in the spine of undefined situation.

In Professor Cheyne's later series of cases three showed abdominal and two thoracic recurrence.

Combining the two series it appears, so far as clinical evidence can show, that in his cases the frequency of abdominal is to that of thoracic recurrence as two to one—an excessive proportion.

Even assuming that in some of these cases epigastric invasion had occurred at the time of operation, it is, in my opinion, probable that in a proportion of the cases a freer downward removal of the deep fascia well below the epigastric angle would have anticipated and prevented invasion of the abdomen.

The Importance of Removing the Upper Part of the Anterior Layer of the Rectus Sheath.

The use of the expression "removal of the pectoral fascia" and the exclusive attention paid to embolic invasion of the axillary glands as the means of dissemination, have led to neglect in the excision of the deep fascia over the lower part of the thorax and the upper part of the abdomen. And it is precisely in the epigastric region that especially complete and careful removal of the deep fascia is most imperatively called for, so as to prevent the access of cancer-cells to the peritoneal cavity. Only in cases of early cancer situated in the upper and outer quadrant of the breast can removal of the epigastric deep fascia be safely omitted.

Removal of Muscle.

The necessity for the removal of a layer of muscle subjacent to the primary growth depends upon the extension of permeation from the fascial lymphatic plexus into its muscular

tributaries (see pp. 87 and 94). As far as possible the layer of muscle removed should attain its maximum thickness just beneath the primary growth, and should become thinner towards the periphery of the operation area. But for several reasons ablation of muscle cannot be carried out in the same strict conformity with the law of centrifugal spread as is possible and desirable in the case of the skin and the deep fascia. For in the first place, once a muscle is invaded by cancer, its contractions probably lead to a wide diffusion of cancer-cells in the direction of its fibres between the muscular bundles, so that the whole muscle must be regarded as suspect. In the second place, it is useless to scoop out a circular portion of muscle on the centrifugal principle because the remaining portions of the muscle will be functionally useless.

The present practice as regards the removal of muscles appears to be correct. The whole of the great pectoral, except in early cases some of its uppermost clavicular fibres, should be removed, according to Halsted's recommendation. The removal of this muscle is essential, not only on account of its close relations with the breast, but also in order to reach the apex of the axilla. The minor pectoral, which is only in direct contact with the breast along its lower border, should be taken away if the case is an advanced one. But it is far more important to remove the digitations of the serratus magnus which lie in direct contact with the deep surface of the breast (see p. 168). This point in the operative treatment of breast-cancer has, I believe, been overlooked. A superficial layer, at any rate, of the digitations of the external oblique which arise from the fifth and sixth ribs, requires removal for a similar reason.

Removal of the Axillary Tissues.

The necessity for a careful dissection of the axilla, and for the complete removal of its fat and glands in one continuous piece with the breast, is generally recognised, and need not here be further emphasized. The details of the dissection may be reserved for discussion in the next chapter.

The Choice of Cases for Operation.

If the accumulation of strikingly favourable statistical results were a legitimate primary aim, there can be no doubt that operation should be refused in all but early cases. But in each case as it comes before him the surgeon has to consider solely the interests of the individual patient concerned, not only in regard to cure, but in regard to the prolongation of life. Now that the immediate risk is so slight it is unfair to refuse operation unless the case is evidently hopeless. Apparently advanced cases sometimes do well, a fact to which Mr. Bland-Sutton has especially drawn attention.* In early cases operation should be urged, in later cases the facts should be laid before the patient or her nearest friends, and the surgeon should be guided by their decision.

Operation should be refused (except in rare cases as a palliative measure for the removal of a foul ulcerating mass) in the following instances:

(*a.*) When the primary growth has attacked the bony thorax.

(*b.*) In the presence of cancer *en cuirasse*, or of subcutaneous nodules or skin-infiltration situated more than two or three inches from the primary growth.

(*c.*) If there is a fixed mass of growth in the axilla, evidently adherent to its walls.

(*d.*) If there is marked œdema of the arm.

(*e.*) If the supra-clavicular glands are enlarged, hard, and fixed.

(*f.*) If there is evidence of visceral or bone metastases.

(*g.*) If there is incurable constitutional disease, tuberculosis or diabetes, for example, likely to be fatal within a few years at most, or to lead to a post-operative fatality.

In seeking for evidence of visceral deposits, examination of the spine for angular curvature should not be omitted. Prior to operating on a cancer of the breast, a careful examination of the epigastric parietes should always be made. The

* Bland-Sutton, "Tumours: Innocent and Malignant."

presence of tenderness or pain in this region should raise the suspicion that epigastric invasion has already occurred; and in such cases the liver should be carefully palpated under the anæsthetic, especially in the epigastric region, before the breast is removed. If any irregular nodular enlargement of the organ is present the operation should be abandoned; for it appears at present hopeless to pursue the cancer into the peritoneal cavity, and anything short of this would be futile in such a case.

The presence of palpable subcutaneous nodules over or below the xiphoid cartilage is an unequivocal indication that epigastric invasion has already taken place, and that operation is useless.

It must never be forgotten that the first sign of epigastric invasion may be found, not in the epigastric region, but in the pelvis, from the gravitation of cancerous particles into it. A vaginal and rectal examination should be made as a routine measure prior to operation. Pelvic pain, enlargement of the ovaries, or induration in Douglas's Pouch, should raise a grave suspicion that the case is beyond the reach of operation.

Certain cases in which formerly operation was refused, are now regarded, subject to the preceding limitations, as coming within its range. (*a*) Scirrhus of the atrophic type should be operated upon except in very old and feeble subjects. (*b*) If the supra-clavicular glands are enlarged and hard, but still mobile, the posterior triangle should be cleared as part of the primary operation. I have not found that this step increases the severity of the procedure to an impracticable extent. Among seventy-six cases of Halsted, which had remained free from recurrence for three or more years, were nine cases in which cancerous supra-clavicular glands had been removed. It is, however, to be borne in mind that, the further embolic supply of cancer-cells being cut off, the supra-clavicular glands in some of these cases might have been able to destroy the young cancerous foci which they at the time contained.

CHAPTER XIII.

A METHOD FOR THE OPERATIVE EXTIRPATION OF BREAST-CANCER.

PARTIAL and incomplete operations on breast cancer, which secure rapid immediate healing at the expense of the patient's future, cannot be too strongly deprecated, and such operations are still frequently practised. On the other hand, such a surgical adventure as exploration of the anterior mediastinum (or even the routine removal of the supra-clavicular glands) seems to offer at the best a very doubtful benefit in exchange for an inevitable risk.

There can be no doubt that the future of breast surgery rests as much with the early diagnosis of doubtful swellings by means of exploratory incision and microscopical examination as with improved methods for the extirpation of fully developed "clinical" carcinoma.

The operation now to be described is, in my opinion, applicable to a large majority of the cases of breast-cancer that present themselves for surgical treatment with well-marked clinical signs of carcinoma. In undoubtedly early cases it is probable that a somewhat less extensive operation will give equally good results. And in old and feeble patients the middle path between the risk of incomplete removal and the risk of a post-operative fatality must be carefully determined and adhered to, with a full recognition of the responsibility involved.

I believe the operation which I practise is more fully in accordance with the facts of dissemination than are any of the methods hitherto in use. I have used the method sufficiently often to recommend it with confidence as perfectly safe in itself, and not unduly severe considering the great issues at stake. But, of course, I cannot yet speak of its remote results.

I would expressly disclaim originality in regard to particular operative details, while claiming it for some of the principles of the method now to be described. Even the removal of the upper part of the anterior layer of the rectus sheath—a step designed to prevent epigastric invasion—has been practised before by various operators and for other reasons, for example, by Mr. Henry Morris and Mr. Pearce Gould at the Middlesex Hospital, by Mr. Symonds at Guy's Hospital, and by Dr. J. H. Pringle in Glasgow.*

Preparation of the Patient.

There are one or two special points which may be mentioned as regards the preparation of the patient. Two vigorous hot baths *per diem* for two or three days prior to operation not only tend to render the skin aseptic, but to make it soft and supple. In cleansing the skin overnight before the compress of one per cent. lysol is applied, care should be taken to rub towards the tumour and not away from it, since many of the lymphatics are filled with cancer-cells, which may not improbably be forced by massage yet further afield. At the time of operation the arm, though well abducted, must not be forcibly stretched upwards, for this, I am convinced, is one cause of persistent axillary pain in the early days of convalesence.

The Choice of Anaesthetic.

In most cases gas or ethyl-chloride, followed by ether, administered with just enough air to avoid cyanosis, are the best agents for inducing anaesthesia. But in my opinion the employment of such a strong circulatory stimulant as ether

* Dr. Pringle's reasons for this step are interesting and suggestive. He believes that there is a downward and inward "tail" of mammary tissue as there is an upward and outward one towards the axilla, both following the line along which supernumerary nipples or mammae are seen. He found it quicker and easier to get out the tissue in this direction by taking away the anterior layer of the rectus sheath, beginning as soon as it showed, and going to the middle line and as far downwards as could be reached. The only criticism I would offer, not of Dr. Pringle's practice but of his theory, is that the line of supernumerary nipples in the examples which I have seen is directed rather towards the umbilicus than towards the epigastric angle.

throughout the operation tends to unnecessary hæmorrhage and to post-operative shock, not manifest during the operation, but showing itself after the patient has been put back to bed. After the skin-incisions have been made, chloroform, or C.E. mixture is the best anaesthetic. A return to ether will rarely be necessary, especially if a very gentle stream of oxygen be continuously administered through a mouth-tube while the operation is going on.

DESCRIPTION OF OPERATION.

The method of operation, while easy enough to demonstrate in the operating theatre, is somewhat difficult to describe clearly in words.

THE CENTRE OF THE GROWTH, *not necessarily the nipple*, MUST BE TAKEN THROUGHOUT AS THE CENTRAL POINT OF THE OPERATION AREA. THE REMOVAL OF THE BREAST IS MERELY A NECESSARY INCIDENT, AND NOT THE SOLE OBJECT, OF THE OPERATION.

The Skin Incision.

The skin incision is only just deep enough to open up the subcutaneous fat without extending through it into the neighbourhood of the deep fascia. It consists of three parts :—

1. A ring incision, as first practised by Mitchell Banks, 4 to 5 inches in diameter, accurately centred on the growth and surrounding it at a safe distance, slightly tailing off into (2) above, and into (3) below.

2. A curvilinear incision for giving access to the axilla. The axilla is opened by turning forward a flap consisting of skin and a thin layer of subcutaneous fat, whose base lies along the anterior axillary fold. The axillary incision begins at the lower edge of the great pectoral, close to its insertion. It ends, also at the lower edge of the great pectoral, by joining the annular incision (1). It crosses the base of the axilla, and marks out an almost semi-circular flap of skin, whose convexity reaches back nearly to the edge of the latissimus dorsi. It affords perfect access to the axilla and good drainage afterwards.

3. A linear incision coming off from the lower and inner part of the annular incision and passing downwards for about two inches along the linea alba. Its object is to give access for the removal of the deep fascia over the upper part of

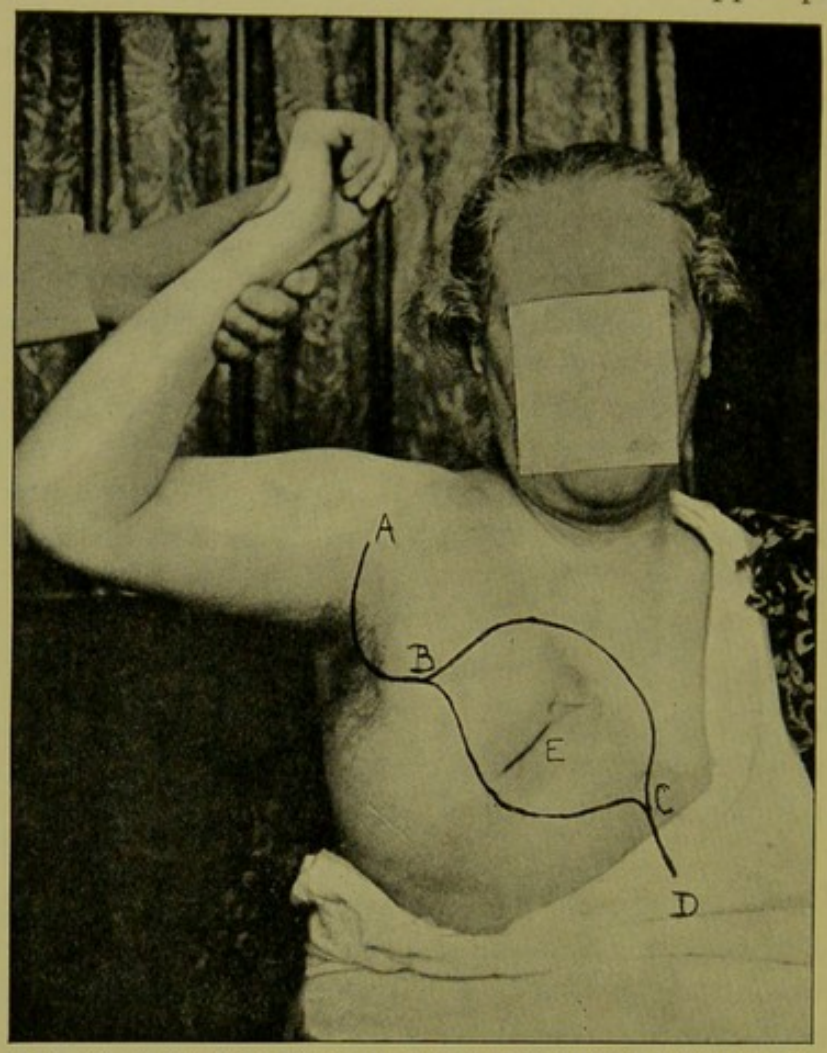


FIG. 44.—THE SKIN INCISION IN THE AUTHOR'S METHOD OF OPERATION FOR ADVANCED CASES OF BREAST-CANCER.

B C is the circular incision with the primary growth at its centre, marking out the area of skin to be removed; A B is the axillary flap-incision; C D the linear prolongation of the incision downwards to the epigastrium; E a pucker in the skin, due to the contraction of the growth.

the abdominal wall. Without it this important step in the operation cannot be properly carried out.

Elevation of the Skin-flaps.

The skin-flaps are next undermined in the mid-plane of the subcutaneous fat until an area of the deeper subcutaneous

fat, forming a circle ten to twelve inches in diameter with the primary growth at its centre (see Fig. 45), is exposed. The exact anatomical limits of this dissection will, of course, vary with the situation of the growth in the breast. The assistant retracts the skin-flaps as they are formed and subsequently keeps them carefully wrapped in hot towels frequently renewed. Neglect of this precaution is likely to be followed by ulceration of the edges of the flaps.

At this period of the operation no attempt should be made to apply artery-forceps to every small bleeding point. Spouting vessels in the deep surface of the skin-flap should be clamped, but bleeding from the exposed surface of subcutaneous fat is sufficiently checked by the pressure of large flat swabs, for nearly all the exposed vessels will again be divided at a deeper level.

Delimitation of the Area of Deep Fascia to be Removed.

An annular incision, marking out the ten-inch circle of deep fascia to be removed, is now carried down to the muscles through the deeper subcutaneous fat close to the base of the skin-flaps, which are meanwhile strongly retracted by the assistant.

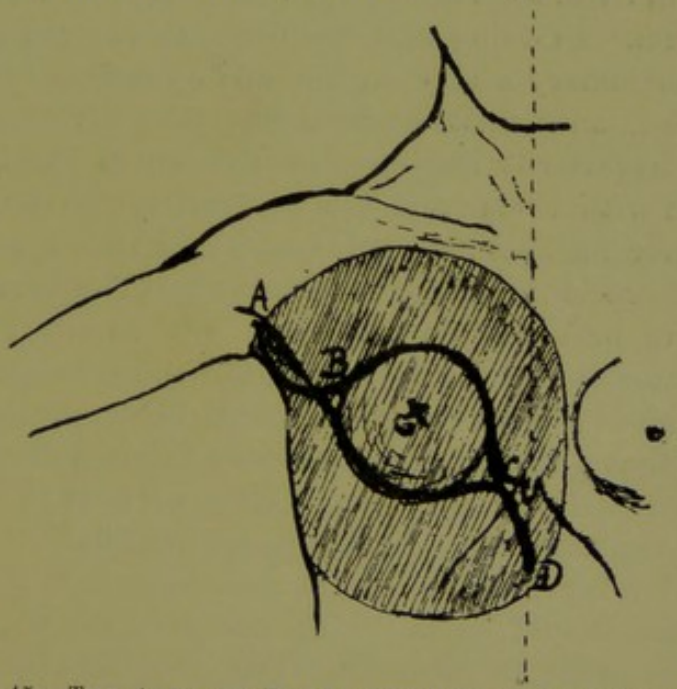


FIG. 45.—THE AREA OF FASCIA REMOVED IN THE AUTHOR'S OPERATION FOR ADVANCED CASES OF BREAST-CANCER.

The shaded area is the area of deep fascia which requires removal. The primary growth is, in this case, situated just above and internal to the nipple. It should always lie at the central point of the area of deep fascia removed.

Elevation of Deep Fascia from the Underlying Muscles.

The circular area of deeper subcutaneous fat and deep fascia, in which lies embedded the presumably permeated area of the fascial lymphatic plexus, is now dissected from the subjacent muscles for some distance from its circumference towards its centre, so as to form a wide marginal fringe of the main mass, consisting of breast, pectoral muscles, and axillary contents, which is to be subsequently removed. The fringe of deep fascia is to be raised up all round the field of operation until the knife reaches either the margin of the great pectoral muscle, the margin of the axillary outlet, or the edge of the breast, as the case may be.

The amount of dissection required varies in different parts of the field of operation. At the upper limit of the field of operation hardly any freeing of the fascia will be requisite, since in this region it will come away with the great pectoral when that muscle is divided at its clavicular origin. Towards the middle line the fascia will usually require dissecting up from the inner margin of the opposite great pectoral and from the sternum. In doing this the perforating branches of the internal mammary artery on the side *opposite* to the growth are divided, and must be secured. The division of these branches necessarily implies also division of the lymphatics which run with them from the pectoral lymphatic plexus to the anterior mediastinal glands, and thus additional security against thoracic invasion is obtained. (The corresponding perforating branches on the same side as the growth are divided later during the detachment of the great pectoral.)

As regards the lower limit of the field of operation, it will be found that a 10-inch circle of deep fascia with the growth at its centre will usually extend well down over the epigastric region of the abdomen. In this part of the field of operation, the anterior layer of the rectus sheath, on both sides of the middle line, should be raised up and removed with the deep fascia. In order to accomplish this, the linea alba must be split from below upwards in the coronal plane. It is particularly in the epigastric region that wide and careful removal of the deep fascia is most imperatively called for, so as to prevent the access of cancer-cells to the peritoneal cavity.

In this part of the field of operation numerous small blood-vessels emerging from the rectus muscle will probably need attention.

Towards the outer side of the field of operation, the fascia must be dissected up from over the anterior edge of the latissimus and from the serratus magnus. Higher up, especially if the growth lies in the outer portion of the breast, the fascia over the inner margin of the deltoid muscle and about the posterior margin of the axillary outlet must be raised if it falls within the circle marked out for removal, although the requisite dissection is difficult and tedious.

Division of Muscles.

If the growth is an early one, or is situated low down in the breast, it is probably safe to leave the uppermost fibres of the pectoralis major near the margin of the deltoid muscle. With this possible exception the whole of the great pectoral needs removal. It is first cut through close to its clavicular attachment, next a finger is inserted beneath the muscle from above, so as to put its fibres on the stretch, and its chondral and sternal attachments are rapidly divided from above downwards close to their origin. The muscle is lifted from the chest and turned outwards, and the external anterior thoracic nerve and the vessels which run with it are divided where they pierce the costo-coracoid membrane.

The pectoralis minor now comes into view, and is best removed, except in early cases. It is divided at its costal origin.

The pectoral muscles are now cut across at their insertion respectively into the humerus and the coracoid process, and the whole mass of tissue is allowed to fall over towards the axilla.

Removal of Axillary Contents.

The costo-coracoid membrane, now freely exposed, is cautiously divided just below the clavicle, and the fat at the extreme apex of the axilla is thus brought into view. It now becomes easy to reach the highest axillary glands—subclavian in the strict sense of the word—which so easily escape notice unless they are carefully looked for. The

axillary vein is sought for in this situation, and is carefully cleared from above downwards. As this dissection proceeds the subscapular vein and other axillary tributaries come into view, and are secured and divided. The subscapular nerves are exposed, isolated, and preserved. The inner and posterior walls of the axilla are cleaned from above downwards, preserving the nerve of Bell, and the mass of tissues is now retained only where the lower and outer part of the breast overlies the serratus magnus. The digitations of this muscle, which lie in direct contact with the deep surface of the breast, should be divided at their origin from the ribs. The whole mass of tissues is now freed and removed by the division, further back towards the scapula, of these same digitations of the serratus magnus. A superficial layer of the digitations of the external oblique, which arise from the fifth and sixth ribs, should also be removed.

The parts removed form a single circular biconvex lens-like mass with thin extensive edges. To its outer side a pyramidal mass of axillary fat and glands is attached. The mass shows a central circular patch of ablated skin on its superficial aspect.

Haemostasis and Drainage.

Any bleeding points which have escaped ligature or forcipressure are now attended to. Two small drainage tubes are inserted through punctures in the extreme base of the skin-flaps, one in the epigastric angle, the other at the posterior margin of the axilla. These tubes are removed at the first dressing twenty-four hours later.

Sutures.

Trial is now made how best the incision may be brought together. The problem varies in each case according to the situation of the growth in the breast, and to the degree of laxity of the skin. The most striking indirect advantage of the operation now becomes evident. The wide removal of the deep fascia so mobilises and frees the surrounding skin that, even after the removal of a 5-inch circle of integument, the edges of the incision can usually be brought together without the use of tension stitches, by a single continuous

suture of fine catgut. Tension in the skin-flaps—the principal cause of prolonged shock, of pain and discomfort to the patient, of impaired circulation in the skin-flaps, and of delayed union and ulceration in the sutured incision — is thus entirely avoided.

Often it will be found best to bring the edges together in tri-radiate fashion, in other cases as a sinuous line. In growths of the upper and outer quadrant some difficulty may be met with in covering the raw area, and in these cases the axillary flap of skin may be pulled inwards to assist in covering the thoracic gap. I have only met with one case in which it was impossible to bring the edges of the incision together—an ulcerated growth of the upper and outer quadrant, in a thin woman with very small breasts and an ill-developed thorax. It appeared in this case that the inward drag of the ulcerated growth upon the surrounding skin had exhausted its elasticity. Moreover, the small size of the thorax and of the breast minimised in this exceptional case the available reserve of skin, so that all the conditions were unfavourable.

An Alternative Method of Fashioning the Skin-flaps.

After the ring-incision in the skin has been made, but before the axillary and epigastric incisions have been marked out, the tedious process of dissecting up the skin-flaps may be avoided by the following manœuvre :—A sharp-pointed narrow knife with a blade three inches long is pushed into the mid plane of the subcutaneous fat from some convenient point in the ring-incision in a direction radially away from the growth, so that the flat of the blade lies parallel to the skin surface. The left hand is now placed flat upon the skin surface, and the assistant pulls the breast over in the direction towards which the handle of the knife is pointing, so as to render the tissues tense. With a sawing movement the knife is now rapidly carried subcutaneously round the whole circumference of the ring-incision, splitting the subcutaneous fat into two layers over an annular area three inches in width on all sides of the skin-incision. The axillary and epigastric skin-incisions are then made, and the operation completed in the usual manner. Great care is necessary to prevent the point of

the knife from coming too near the skin surface and thus scoring the skin-flap and imperilling its nutrition, and in spite of the saving of time which it secures, I hesitate to recommend "subcutaneous transfixion" as a routine method for forming the skin-flaps. It should only be used when there is a fairly thick layer of subcutaneous fat, and when the operator is confident that he can avoid scoring the flaps with the point of his knife.

Constitutional Effects of the Operation.

The operation for breast-cancer inevitably produces some degree of immediate shock, and perhaps this is slightly increased by the operative method which I have described. I have never, however, seen dangerous shock during the operation. For its prevention it is, I believe, important to keep the skin flaps, and the thorax generally, covered with hot towels so far as the operator's convenience will allow. The persistence of shock for some days after the operation appears to depend almost entirely on tension in the skin flaps, and the pain associated therewith. At any rate, I have noticed, paradoxical as it may appear, that the shock of the operation just described passes off much more quickly than the shock which follows the less extensive operations described in the text-books, in which tension sutures are necessary for the approximation of the skin edges. Recovery is rapid, and up to the present I have not lost a case.

Complications.

The complications which I have met with after this operation are infrequent and not serious. Suppuration of such an extensive wound would of course be attended by considerable risk, but should be a very rare event if proper precautions are taken. Thiersch grafting may be necessary in rare cases. I have had to resort to it twice, once from inability to cover the gap left by the operation, and once for sloughing, over an area of about four square inches, of the apex of one of the flaps. The patient in this case was a stout bronchitic subject with congested fascial venules. This is the only case in which I have met with sloughing of the skin-flaps, and I ascribe it to

the tension produced by the drag of the very heavy and pendulous remaining breast, which had been undermined at its inner edge in the course of the operation.

The only complication at all frequently met with is slight ulceration of the immediate edges of the incision of varying extent. This may sometimes delay complete healing for several weeks. It is not accompanied by suppuration, and seems to be due to a local invasion of the imperfectly vitalised tissues by the bacteria of the skin.

After-treatment.

The arm is not included in the bandage, but is placed in a sling. One injection of morphia may be necessary on the night of operation. A mixture containing small doses of digitalis and brandy may in feeble subjects be given for a few days. If there is any history of, or tendency towards, bronchitis the patient should be placed in a semi-sitting posture from the evening of the day of operation. The dressing is changed, and the drainage tubes removed, after twenty-four hours. The patient usually gets up on the fifth day. Only slight abduction of the arm should be permitted until the stitches, unless consisting of absorbable catgut, are removed on the tenth day. Free use of the arm in abduction prior to this period is apt to be followed by the collection of serum beneath the flaps, or by gaping of the edges of the wound. A serous collection is also likely to form beneath the flaps in the epigastric region if the bandages are allowed to become loose. The patient is usually able to leave the hospital or home in fourteen to twenty-one days. After the end of the third week systematic measures must be taken to mobilise the scar upon the chest. For this purpose a course of massage, for the most part applied transversely to the direction of the scar, is useful in addition to the exercises usually prescribed.

Of late I have recommended a short course of X-ray treatment as a prophylactic against recurrence after the operation. An exposure of average duration is given twice a week for a period of not longer than three weeks. It is, I think, doubtful whether a more extended course is advisable.

APPENDIX.

ON LYMPHATIC PERMEATION AS A FACTOR IN THE DISSEMINATION OF MELANOTIC SARCOMA, WITH A NOTE ON OPERATIVE TREATMENT.*

I. Introductory.

There are certain exceptions to the rule that sarcomata do not invade the lymphatic glands. In sarcoma of the testis and of the tonsil, in lympho-sarcoma, and in melanotic sarcoma wherever it is situated, the lymphatic glands are frequently involved. Clearly therefore the lymphatic channels are concerned in the dissemination of these exceptional forms of sarcoma.

The investigation now to be described was undertaken with two objects, firstly, to determine what share lymphatic spread takes in the dissemination of sarcomata which are prone to invade lymphatic glands; and secondly, to find whether the process of permeation, which I have described as taking a predominant part in the dissemination of carcinoma, can also be detected in such sarcomata. Sarcoma of the melanotic variety was chosen for investigation because its commonly intense black colour renders the unequivocal recognition of very minute foci of growth easy both to the naked eye and microscopically. Moreover, this variety of sarcoma, frequently arising in regions whose lymphatics are tributary to the fascial lymphatic plexus, often gives rise, like carcinoma of the breast, to subcutaneous nodules; and an accurate comparison of the mode of spread of these two varieties of growth in identical tissues thus becomes possible.

Owing to the rarity of melanotic sarcoma, and the somewhat tedious method of investigation employed, this paper deals only with one case.

* A paper reprinted from Vol. vii. of the Archives of the Middlesex Hospital, by kind permission of the Cancer Investigation Committee.

II. Detailed Description of Case.

Abstract of Necropsy.—Necropsy No. 186, The Middlesex Hospital, 1905. The body is that of an emaciated woman, aged thirty-four. At the insertion of the right tendo Achillis is a small healthy linear scar, where the primary melanotic sarcoma was excised. In Scarpa's triangle on the right side is a considerable mass in the situation of the femoral glands. Beneath the skin over and around this mass are very numerous discrete black nodular growths, occupying an area roughly circular in shape and perhaps eight inches in diameter (see Fig. 46). The growths become smaller in all directions the further they are situated from the femoral glands, until apparently healthy skin is reached.

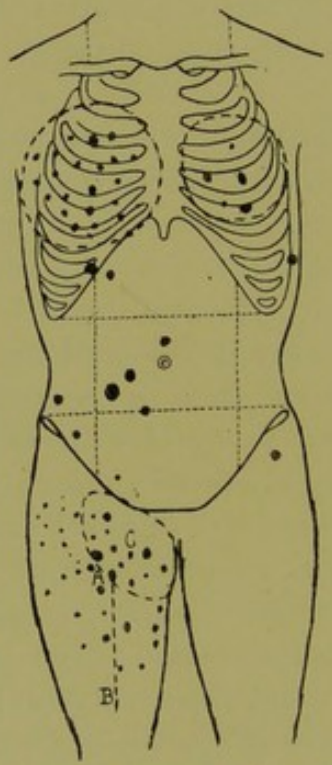


Fig. 46 shows all the visible subcutaneous nodules of melanotic growth present in the anterior aspect of the body, except one on the face.

The dotted line A B shows the position and extent of the strip of tissue removed for examination. The dotted circles in the mammary region represent prominent masses of secondary growth in the breasts.

Note that the growth was on the right heel, and that most of the secondary nodules are situated on the right side of the body.

On the back, at the level of the tenth dorsal vertebra, there is a patch three inches square studded with similar cutaneous growths.

The right breast shows enormous enlargement, and in the skin over the breast are many similar growths. The left breast, though smaller, is in a like condition. Scattered over the front of the thorax and the abdomen are numerous subcutaneous nodules, and there is one on the face in the left malar region. There is far more growth on the right side of the body than on the left. No deposits are present in the skin and subcutaneous tissue of the left leg below the level of the symphysis pubis.

There are numerous deposits in the calvaria; a few small nodules are present in the brain, and in the thyroid body.

Several deposits are found on the posterior surface of the sternum. The cardiac muscle contains numerous nodules, and a few are scattered throughout the lungs.

The liver weighed 101½ ounces. The only abdominal viscera free from new growth are the spleen, ureters, bladder, and stomach. Numerous nodules are pendent from the mucosa of the intestines.

The left femur shows a fracture one inch below the great trochanter, surrounded by a mass of non-pigmented new growth. All the muscles examined show minute specks of melanotic pigment. As regards the lymphatic glands, growth is found in the right femoral and internal iliac glands (and to a less extent in the lumbar glands), and in the cervical and axillary glands on both sides.

For the investigation of lymphatic spread in this case it was natural to choose the tissues in the neighbourhood of the largest mass of lymphatic glands, that is to say, the tissues of the right groin. A strip of the parietal tissues passing down the thigh from this mass of glands was removed for examination.

Naked-eye Description of Strip.—The strip of tissues examined measured 17 cm. in length, and extended from the lower edge of the mass of growth which occupied the situation of the inguinal glands vertically down the anterior surface of the thigh to a point about 3 in. above the knee. It traversed

and passed well below the circum-inguinal area of visible subcutaneous nodules of growth (see Fig. 46).

The strip included skin, subcutaneous fat, deep fascia, and a thin layer of muscle. It was frozen, and subdivided longitudinally into three thinner strips. One of these was submitted to microscopic examination, while the two other strips, each about 3 mm. thick, were mounted as naked-eye specimens.

Method of Preparation.—The strips were prepared by a modification of a method which I first employed in 1904 for demonstrating carcinomatous nodules in the parietal tissues in cases of breast-cancer. For this purpose long strips of the skin and subjacent parietal tissues radiating in any selected direction from the primary growth were cut from the cadaver, and were subsequently stained and rendered translucent.*

The staining method employed had the defect common to all stains, that it is not specific for cancerous tissues. Moreover time has shown that the specimens, when mounted in xylol for preservation in a museum, undergo continuous shrinkage, and lose their purity of colour, so that after the lapse of two years their deterioration is marked.

Melanotic sarcoma offers an ideal field for the application of this method in a simplified form, because the specimens can be mounted in an absolutely unstained condition. The dark colouration of this particular variety of growth is the equivalent of a specific stain for malignant tissues, a desideratum which is at present lacking in the case of other growths.

The two strips having been frozen and cut, were placed in methylated spirit for twelve hours, and subsequently in acetone for a similar period; they were thence transferred to xylol for a few hours, and finally mounted in liquid paraffin (parolein, B. W. & Co.) as museum specimens in flat-sided jars.

The use of acetone as a dehydrating agent in place of absolute alcohol was suggested to me by Dr. Victor Bonney, while the employment of liquid paraffin as a mounting fluid is an improvement due to Mr. Cecil Rowntree. In contrast

* The original method is described on p. 29.

to xylol, liquid paraffin is not appreciably volatile; moreover, it is perfectly transparent, and tends rather to make the specimen soft and pliable than to harden it. The only remaining doubt, whether it ultimately exercises any deleterious influence on the specimen or is itself discoloured by the action of light, can only be settled by the lapse of time.

Naked-eye Description of Radial Strip. — Subject, of course, to microscopic confirmation, the strip affords to the naked eye a beautiful demonstration of the process of permeation (see Fig. 47). At the proximal end of the strip the translucency of the tissues is blurred by an abnormal excess of adventitious fibrous tissue in the subcutaneous fat, an index to the inflammatory reaction excited by the growth. Here large nodular masses and cords of growth are seen in the various layers, but the finer network of black lines seen towards the distal end of the strip is absent.

The salient features of the strip may be best expressed in the following table of measurements, which are all taken from the upper end of the strip:—

	Centimetres.
Total length of strip	17
Retiform (intravascular) invasion of deep fascia and deepest layers of the subcutaneous fat present in the entire length . . .	17
Nodular invasion of the deep fascia . . .	13·6
Retiform (intravascular ?) invasion of the skin	12
Nodular invasion of the skin	10
Nodular invasion of the muscle . . .	9·5
Nodules forming palpable and visible prominences on the skin surface	6·5

Microscopic Description of Strip.—The various blocks into which the original strip was divided will now be described in order from the proximal to the distal end. It will be noted that a gradual and regular change takes place as the strip passes under review. At the proximal end are large nodules, with invasion of the arteries and veins as well as the lymphatics. At the distal end no invaded blood vessels are to be found, nor are large nodules of growth present; but the lymphatics are filled by fine cylinders of growth.

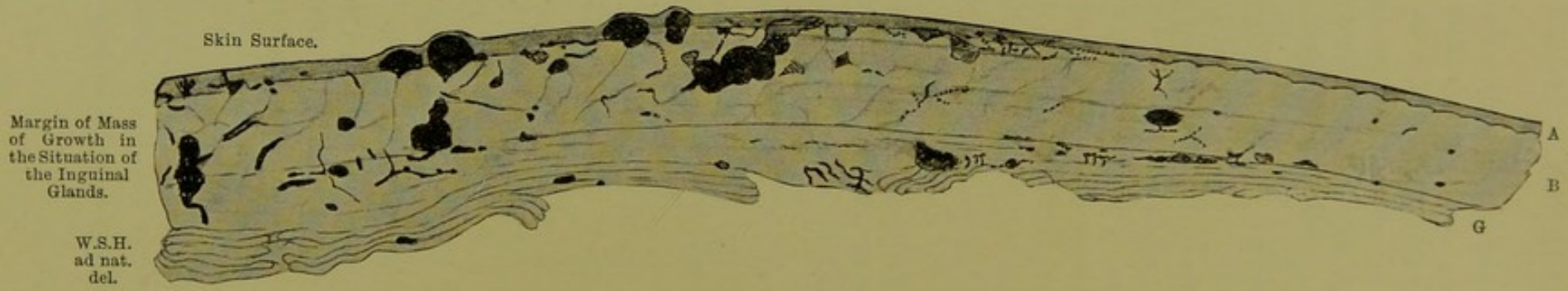


FIG. 47.—Drawing, natural size, of a translucent strip of the skin and underlying tissues taken in a radial direction from the mass of growth in the situation of the inguinal glands, to demonstrate the centrifugal spread of permeation. Note that the growth extends much further along the deep fascia than along the skin or in the muscle.

A, skin ; B, subcutaneous fat, separated by the deep fascia from G, a thin layer of muscle.

The presence of inflammatory changes at the proximal end of the strip, and their absence at the distal end, are to be especially noted, as indicating that a process analogous to the "perilymphatic fibrosis," which obliterates permeated carcinomatous lymphatics, occurs also in melanotic sarcoma.

Block 1.—In this block there is invasion of arteries and veins, together with nodular invasion of the tissues; but there is no reticulum of small permeated lymphatics. It is probable that many of the originally permeated lymphatics have been destroyed by perilymphatic fibrosis, for at this, the proximal

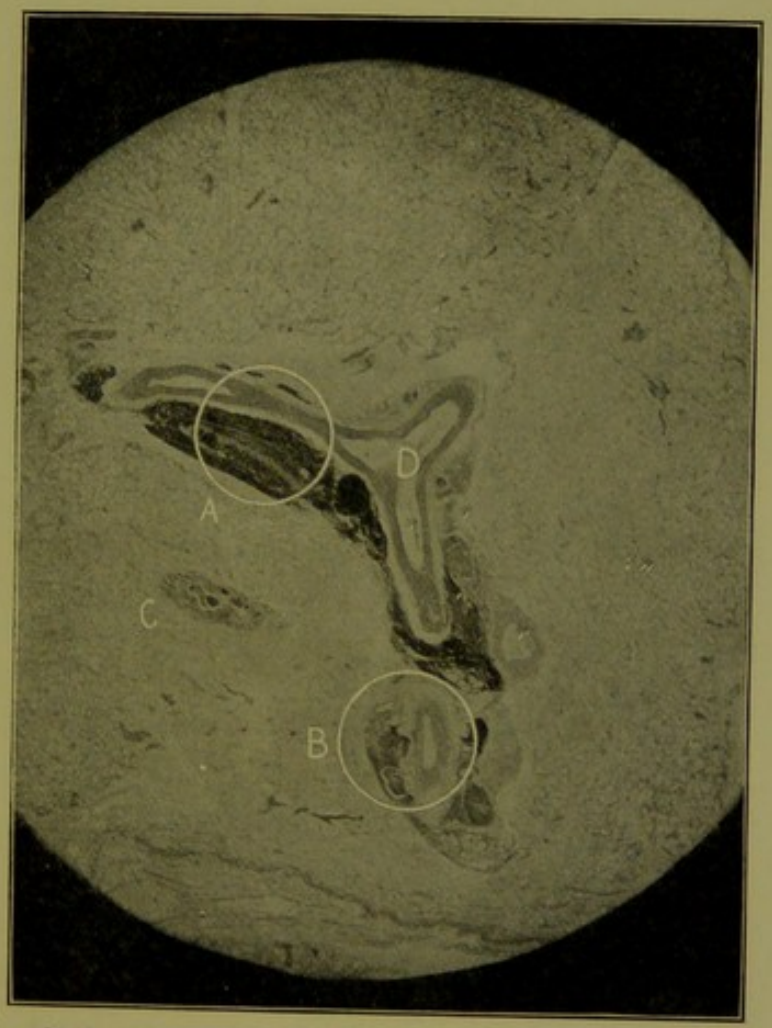


FIG. 48, × 30, from the proximal end of the strip near the mass of growth which represented the inguinal glands, shows a cylindrical cord of melanotic growth, lying unencapsuled in the periarterial tissues, and replacing the comitant venous and lymphatic vessels.

D is the artery, C a small vein containing a cylinder of degenerate growth infiltrated by leucocytes. The circles A and B show the situation of Figs. 49 and 53.

end of the section, the subcutaneous tissues appear even to the naked eye to be abnormally rich in adventitious fibrous tissue.

Muscle.—Absent from the section.

Deep Fascia.—Only one focus of growth is present, a cord which probably represents a large lymphatic, for it lies not far from a normal small artery and vein.

Subcutaneous Tissues.—In the deeper subcutaneous fat is a normal artery of considerable size, accompanied by a cord of growth (see Fig. 48), which certainly represents the vein, for in it can be seen embedded remains of muscular

FIG. 49, × 160, represents, highly magnified, the upper circle A in Fig. 48. Above is seen in oblique section a normal artery A A. Accompanying this artery and below it is a cord-like cylinder of growth G G G. That G G G represents the vein which originally ran with the artery is shown by the presence within it of a well-marked band of unstriated muscle M M, doubtless a relic of the wall of the vein, which itself was invaded originally from adjacent permeated lymphatics (see Fig. 50).

tissue (see Fig. 49). This cord probably replaces also the comitant lymphatics of the artery in question.

More superficially is an artery, unaccompanied by a vein, which lies in the plane of the section for a considerable distance. It is more or less filled, along the whole of its visible portion, with melanotic growth. It is directed towards a region where two nodules of macroscropic size lie in the subcutaneous fat a little distance below the skin.

Some very minute foci of obsolescent growth, enveloped in inflammatory round cells, are present in the fibrous periarterial tissues.

The fibrous septa which join the skin to the deep fascia, besides presenting one or two minute foci of vigorous sarcoma cells, are littered along their length with fine granules of melanotic pigment, and with very degenerate but still recognisable sarcoma cells.

Skin.—The skin invasion is not uniform, but has occurred at points where the fibrous septa join it. The terminal subdermal expansions of these fibrous septa are densely infiltrated by sarcoma cells.

Block 2.—No arterial invasion is present in this block. Otherwise the appearances are similar to those in Block 1.

Muscle.—Absent from the section.

Deep Fascia.—One or two groups of sarcoma cells, densely enveloped by inflammatory round cells, are present in the deep fascia. A larger aggregation of sarcoma cells, which has slightly infiltrated the overlying fat, is in an advanced stage of degeneration, and in places shows actual infiltration by inflammatory cells.

Subcutaneous Tissue.—The most prominent object in the subcutaneous fat is a large macroscopic nodule of growth, in parts degenerate and penetrated by round cells. Embedded in the centre of this mass are two small arteries, whose muscular coats show commencing infiltration by the growth which surrounds them. The lumen of these vessels is free from growth.

Other smaller nodules of growth are present in the subcutaneous tissues, along the course of the fibrous septa. One minute cord-like mass of growth is very degenerate. Its cells stain badly, and it is both surrounded and infiltrated by

deeply-stained round cells. This focus probably represents an intermediate stage in the process of perilymphatic fibrosis, which had destroyed the smaller permeated lymphatics of the two sections 1 and 2.

Skin.—The skin of this section presents three large nodules of deeply pigmented growth. In addition to these nodules the sub-dermal expansions of several of the fibrous septa show infiltration by degenerate growth, with dense collections of leucocytes around the invaded septa.

Block 3.—The characteristic feature of this section is the large number of inflammatory round cells which are present. They are not diffused throughout the tissues, but are localised in large numbers both in the blood-vessels and also in the perivascular tissues.

Muscle.—Absent from the section.

Deep Fascia.—Absent from the section.

Subcutaneous Fat.—In the deepest layer of the subcutaneous tissue is an artery partially filled by growth. The muscular coat is in places infiltrated in its whole thickness by sarcoma cells. Outside the artery are a few recognisable sarcoma cells mixed with round-celled infiltration. The appearances are consistent either with embolism and infiltration of the arterial wall from within, or with penetration of its wall from an adjoining permeated lymphatic which has subsequently undergone fibrosis.

At various points along the fibrous septa are seen in transverse section relatively large thin-walled vessels lined by endothelium. They possess no definite muscular wall, and are filled by growth. Almost certainly they represent distended lymphatics.

Here and there are small dense localised collections of leucocytes. In some of these aggregations a few degenerate sarcoma cells and melanin granules can be distinctly recognised.

Skin.—The skin contains two large nodules of growth. It is also in places microscopically infiltrated, but not along its whole length.

Block 4.—This block, like the preceding one, shows large numbers of inflammatory round cells in and around the blood vessels.

Muscle, Deep Fascia.—Absent from the section.

Subcutaneous Tissues.—Near the deep fascia is a large artery with a group of sarcomatous cells lying free in the lumen. Towards the other end of the section are a normal small artery and vein, accompanied by a cord of growth which appears to represent a lymphatic. The middle layer of the subcutaneous tissue is occupied by large confluent nodules of growth. The terminal sub-dermal expansions of two of the fibrous septa are infiltrated by growth.

Skin.—The skin is practically free from growth, showing merely one or two endothelial spaces (distended lymphatics) containing sarcoma cells.

Block 5.—Exudation of round cells is still present, but to a much less extent than in the preceding sections. The arteries in the section are normal.

Muscle.—A thin layer of muscle, which forms the lower margin of the specimen is entirely free from growth.

Deep Fascia.—Five foci of growth are spaced out along the deep fascia. They lie within small endothelial-lined spaces, some of which are cut longitudinally, others transversely. Normal blood-vessels can in places be seen closely adjacent to these spaces, which undoubtedly are lymphatics.

Subcutaneous Tissues.—Intravascular foci of growth, in places beginning to infiltrate the surrounding tissues, are sparsely scattered along the fibrous septa of the subcutaneous fat. The vessels containing these foci are very thin-walled, and possess no definite muscular tissue. A slight excess of round cells is present in the perivascular tissues. No large nodules are present in the section.

Skin.—A layer of skin is not present along the whole length of the section. At one point, where a fibrous septum runs up to the dermis, there is commencing interstitial infiltration of the fibrous tissue of the dermis. A large permeated lymphatic is present near this point.

Block 6.—A small series of sections was cut from this block. No invaded blood vessels were found in it anywhere.

Muscle.—The muscular layer was free from growth.

Deep Fascia.—About thirteen small foci of growth were spaced out at intervals along the course of the deep fascia, lying either upon its surface or in its substance. Most of these foci appeared to represent small lymphatic vessels, but

their endothelial lining was not clearly traceable. One large endothelium-lined space, without any muscular tissue in its wall was clearly recognisable as a lymphatic. It contained a mass of degenerate growth, penetrated almost throughout by inflammatory round cells, which were also present in abnormal numbers just outside its wall. Not far from this large lymphatic a small artery and vein, both normal and seen in cross section, were accompanied by two permeated lymphatics containing vigorous sarcoma cells. An exactly similar focus of growth—a normal artery and vein with two permeated lymphatics—is present on the other side of the large lymphatic described earlier (see Fig. 51). There is a moderate amount of perilymphatic leucocytosis round some of the permeated fascial lymphatics.

Subcutaneous Fat.—Here and there in the course of the fibrous septa minute cords of growth are seen cut across either transversely or obliquely. There seems to be an excess of fibrous tissue around these foci, and many round cells are present—not only in the immediate neighbourhood but actually within the sarcomatous tissue. These cords of growth appear to represent permeated lymphatics in an early stage of fibrosis.

Skin.—The dermis shows slight infiltration at one or two points in its deepest layer.

Block 7.—This section, like the preceding one, is characterised by the presence of numerous intravascular (intralymphatic) foci of growth spaced out along the whole length of the deep fascia, while the subcutaneous tissue is relatively free from growth. There is no excess of round cells in the tissues.

Muscle.—Only a few shreds of muscle are present in the section. They are free from growth.

Deep Fascia.—About six foci of growth, consisting either of groups of endothelium-lined spaces full of sarcoma cells, or of minute nodules lying in the tissues, are present along the deep fascia. At the proximal end of the section there is a nodule of non-pigmented growth which envelops a small artery and is infiltrating its wall. The vessel contains normal red corpuscles. Next comes a group of minute branching spaces containing growth, lying between the fibrous bundles of the deep fascia. Some of these are lined by definite

endothelium. These are succeeded, as the section passes under review, by a small nodule of growth which is beginning to infiltrate the fat overlying the deep fascia. Next comes a small normal artery, seen in longitudinal section, accompanied by minute cords of growth, which in places lie definitely within endothelial walls. A normal vein is seen in cross section close to the artery.

Subcutaneous Fat.—There is very little growth in the subcutaneous fat. Five or six foci are present, all minute. Some of these lie free in the tissues, others are enclosed in thin endothelial walls. The arteries and veins appear normal.

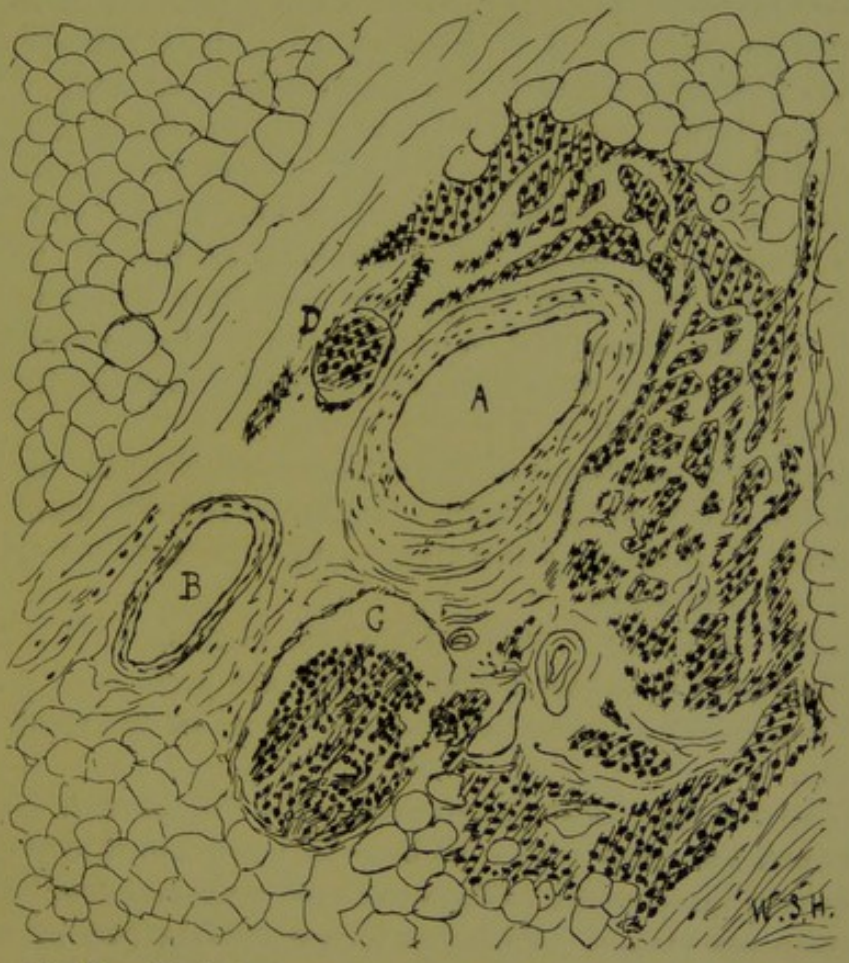


FIG. 50.—From block 8, close to the deep fascia. 1 in. obj., No. 8 oc.

At this point the growth has permeated the lymphatics and is infiltrating the tissues around, but has not yet penetrated to the interior of the blood-vessels.

A is an artery, B a vein, both normal. C is an endothelium-lined space (lymphatic), permeated by growth which has burst through its walls. D is a permeated lymphatic whose wall is still unruptured.

Skin.—The skin is absent from the section except at one point, where a group of sarcoma cells lie within a space in the dermis, probably a lymphatic.

Block 8.—Inflammatory changes are almost entirely absent, that is to say, there is slight, if any, excess of round cells in the tissues.

Muscle.—At one point, about the middle of the section, there is a microscopic collection of sarcoma cells just beneath the surface of the muscle, which is elsewhere free from invasion.

Deep Fascia.—At the proximal end of the section there is a microscopic nodule of diffuse growth which has infiltrated the deep fascia to its deep surface. Opposite the point where the intravascular focus is situated there is a collection of sarcoma cells just beneath the deep fascia. At each of two other foci lying just superficial to the deep fascia (Fig. 50), the growth has infiltrated the walls of two permeated lymphatics, and is beginning to envelop the artery and vein which accompany them. The three other foci of growth present upon the deep fascia are definitely intravascular. Near one of these foci normal minute blood-vessels are visible. There can, therefore, be no doubt that the invaded vessels are lymphatics.

Subcutaneous Tissue.—The subcutaneous fat presents only two minute foci, one of which is beginning to infiltrate the fat, the other is apparently intralymphatic. No invaded arteries or veins are present.

Skin.—The skin is absent from this section.

Block 9.—No invaded blood-vessels are present.

Muscle.—The layer of muscle present is free from growth.

Deep Fascia.—Two intravascular foci of growth are present upon the deep fascia. These foci are cross-sections of permeated lymphatics. Close to them a normal small artery and vein are visible. Very few leucocytes are present in the neighbourhood (see Fig. 52).

Subcutaneous Tissue.—Two microscopic foci, not definitely intravascular, are present in the subcutaneous tissue.

Skin.—The skin is wanting at this, the distal end of the strip examined.

III.—A Discussion of the Data Recorded in Section II.

Local Dissemination Around the Right Inguinal Glands.

The spread of subcutaneous nodules in all directions from the invaded mass of inguinal glands (see Fig. 46), indicates the working of a process of local centrifugal spread from point to point around these glands. The nature of this process is made clear by the microscopic findings which have just been described. Its various stages, from the most advanced to the earliest, are seen successively as the selected radial section is traced outwards from the centre of the mass of glands. Since the strip was taken down the limb, and therefore against the flow of lymph, the force of the lymph-stream can have taken no share in this process of local centrifugal dissemination, at any rate in the particular radial section examined.

It is obvious, both from Fig. 47 and from the microscopic sections, that the process is one of continuous growth of sarcoma along the vessels. And since towards the distal end of the strip only the lymphatic vessels are invaded, and the blood-vessels are normal, it is clear that lymphatic permeation is the initial process in the local centrifugal dissemination which we are discussing, and that invasion of the blood-vessels—present only at the proximal end of the strip—is a secondary consequence in point of time, though not in point of importance.

Invasion of Blood Vessels from Comitant Permeated Lymphatics.

The tendency of melanotic sarcoma to spread along the perivascular tissues immediately outside the blood-vessels has been noticed by Borst. His explanation of the fact is a teleological one, namely, that blood is a necessary food for the production of melanin, and that consequently the sarcoma cells are attracted towards the blood vessels by a kind of chemiotaxis. The true explanation appears to be a simple anatomical fact. The lymphatic vessels, along which permeation extends, usually run in company with arteries and veins.

Figs. 48 to 52 show the various events which lead to the invasion first of veins, and later of arteries, from comitant

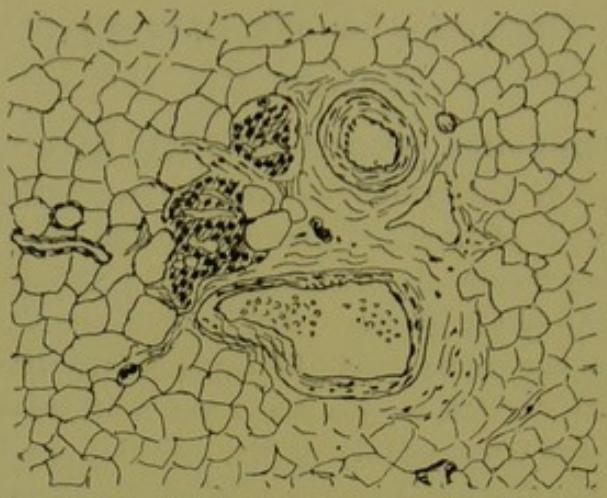


FIG. 51.—From Block 5, close to the deep fascia, ⅔ obj. No. 8 ocular.

A normal artery and vein are accompanied by two microscopic cords of growth, which doubtless represent their comitant lymphatics.

To show that lymphatic invasion precedes invasion of the blood-vessels.

permeated lymphatics. In Fig. 52, taken from the distal extremity of the strip (Block 9), a permeated lymphatic is seen lying near a small artery and vein. Fig. 51 (Block 5) shows two permeated lymphatics lying near normal blood-vessels. Fig. 50 shows the rupture of permeated lymphatics and the proliferation of the sarcoma cells around the walls of the accompanying artery and vein. In Fig. 48 the vein has been infiltrated and destroyed by sarcoma, and portions of its muscular wall are embedded in a cord of growth which accompanies the

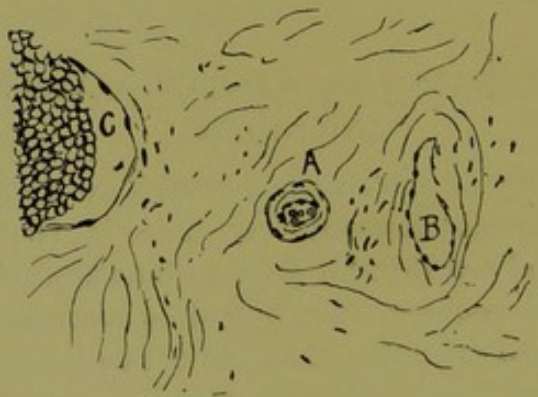


FIG. 52.—From Block 10, ⅔ obj. No. 8 ocular.

The remotest fascial focus present in the strip represented in Fig. 47. A is an arteriole containing blood corpuscles, B is a venule. Both are free from growth.

C is a mass of sarcomatous tissue, circular in section, bounded on one side by a space lined by endothelium, which appears to be a ruptured lymphatic.

No invaded blood-vessels were present anywhere in the slide from which this section was taken. Lymphatic invasion is thus shown to precede blood-invasion.

artery. The artery itself remains intact. The last stage of the process is demonstrated in another field of the same slide, where an artery filled by growth can be seen.

The Question of Spread along the Skin.

A glance at Fig. 47 shows that the skin is not invaded nearly so widely as the deep fascia. As in carcinoma of the breast, the question arises how invasion of the skin occurs. Does the growth spread along the hypothetical "deep cutaneous" lymphatic plexus at the junction of the dermis with the sub-cutaneous fat, as was formerly assumed to be the case in breast cancer? Between points situated 10 and 12 cm. along the strip a definite meshwork of black lines in this place can be seen (Fig. 47), and a superficial glance suggests that this network is the permeated "deep cutaneous plexus," and that the growth is in fact spreading slowly in this plane as well as in the plane of the deep fascia.

Closer inspection shows the error of the supposition. Just beyond the furthest point of invasion of the skin, the growth is seen creeping up to the skin from below, against the lymph stream, along the vertical tributaries which convey lymph from the skin to the lymphatic plexus of the deep fascia. The fallacious appearance of a permeated deep cutaneous plexus is evidently only a further stage of this process. As Sappey showed, the lymphatic vessels coming from the skin, though they freely interlace, do not at the deep aspect of the dermis form a true plexus. They simply interlace like the entangled boughs of adjacent trees in a thick wood. The only cutaneous lymphatic plexus is the sub-papillary plexus.

As in carcinoma, the layers adjoining the plane of the main (deep fascial) lymphatic plexus, are attacked by the upstream extension of permeation along the tributary lymphatics of the fascial plexus.

Regressive Changes in Melanotic Sarcoma.

On reading the detailed microscopic description of the strip given on pp. 207–216, it is obvious that three zones can be distinguished: (*a*) A proximal zone where permeated lymphatics have been to a large extent destroyed. In this zone much adventitious fibrous tissue is present. (*b*) A zone

characterised by the presence of large numbers of round cells, around the sarcomatous foci and within the vessels. (*c*) A distal zone where no inflammatory reaction to the process of permeation has yet taken place. It thus appears that reparative processes, inadequate for cure, are not absent in melanotic sarcoma. Lymphatics and veins permeated by melanotic sarcoma may undergo destruction if the patient lives long enough. Although the mere presence of sarcomatous elements in normal tissues does not excite any inflammatory reaction, yet when the sarcoma cells become degenerate or exert

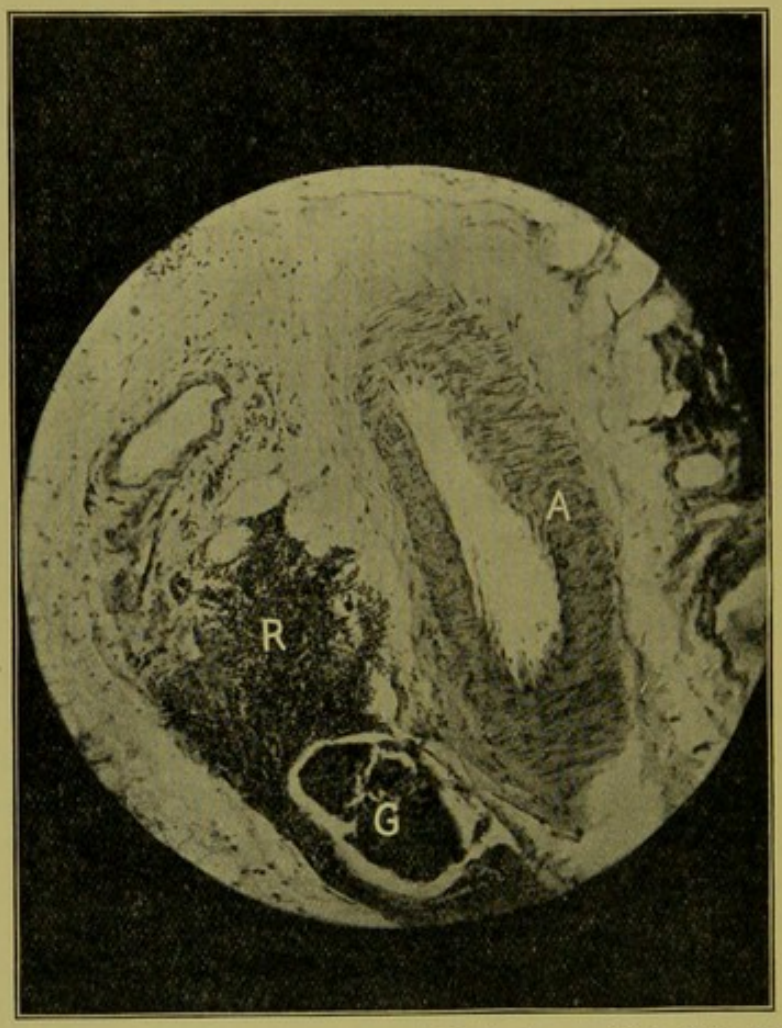


FIG. 53, × 160, represents highly magnified the lower circle B in Fig. 48, and illustrates the reparative processes which occur even in very malignant growths. A is a normal artery, G a mass of growth lying in a space without definite walls, which may be an artefact of the hardening process, but in any case probably represents a ruptured lymphatic or vein. The growth G is surrounded by a very dense collection of inflammatory round cells R. In other parts of the section from which Fig. 53 is derived the later stages of perilymphatic fibrosis could be traced.

mechanical pressure, an inflammatory reaction occurs, which may end in the encapsulation and destruction of the sarcomatous tissue. Even metastases visible to the naked eye may probably in this way be occasionally destroyed. Borst has already drawn attention to the regressive changes which may occur in melanotic sarcoma. Fig. 53 shows a dense mass of inflammatory round cells surrounding and destroying a focus of growth.

Conclusions from Examination of the Tissues in the Inguinal Region.

1. From the fairly regular distribution of skin nodules around the embolically invaded right inguinal glands, it may be inferred that a process of local centrifugal spread independent of the direction of the lymph current, took place around these glands as a focus.

Examination of a radial strip of the parietal tissues extending from these glands showed :—

2. That permeation of the lymphatics is the principal agent in this local centrifugal spread, and that it occurs primarily and most extensively in the plane of the deep fascial lymphatic plexus.

3. Invasion of skin and muscle is due to up-stream permeation of the lymphatics which carry lymph from these layers to the fascial lymphatic plexus.

4. Owing to the fact that arteries and veins usually run in close contiguity to lymphatic vessels, lymphatic permeation is followed by infiltration of the walls of veins, and later of arteries, and by intrusion of the growth into the lumen of the blood-vessels. The importance of invasion of the veins with regard to pulmonary and systemic dissemination is obvious.

5. The order in time of these various events is deduced from the orderly sequence of processes seen as the strip of tissues is traced from its distal end towards the mass of glands which formed the local centre of infection.

6. Regressive changes, due to inflammation excited by the growth, may occur in melanotic sarcoma.

The Share of Embolism in producing the Metastases.

The direct evidence that the majority of the skin nodules present did not originate from emboli carried by the blood-stream has already been adduced. It is interesting to note that nearly all the subcutaneous nodules present were situated on the same side as the primary growth. This distribution is inconsistent with the embolic origin of these particular secondary growths, and strongly suggests a process of local spread, from point to point. On the other hand it is probable that most of the visceral deposits, perhaps those in the breasts, and a few of the subcutaneous nodules, took their origin in blood embolism. Such an embolic origin could be clearly traced in the kidneys, where the glomerular tufts were occupied in places by melanotic material, which at other points had burst into Bowman's capsule. Although "tissue-predisposition" is doubtless, as Mr. Stephen Paget showed, a factor in the survival of embolised fragments of growth, it is difficult to explain on these lines the relative freedom from metastases of the subcutaneous tissues of the left side, as compared with those of the right side.

As soon as the local spread in the lymphatics round the embolically invaded right femoral glands attained a radius of spread reaching to the level of the umbilicus—the dividing line between the territory of the inguinal and the axillary glands—embolic invasion of the axillary glands would occur. Local centrifugal spread around these glands, reaching a maximum in the rich lymphatic network of the breast, would account for the subcutaneous nodules present over the chest, and for the mammary masses of growth.

Dissemination around a Primary Melanotic Sarcoma.

Since in this case the primary growth had been removed by operation, it was not possible to study centrifugal lymphatic spread around the primary focus, but only around a secondary focus—the embolically invaded inguinal glands of the right side. And as these glands form the centre of important converging lymphatic trunks, it is probable that permeation might travel from them centrifugally with greater

rapidity than from a primary focus situated in a region more sparingly supplied with lymphatic communications. But for all practical purposes the conclusions arrived at from considering dissemination around an embolically invaded gland, are applicable to dissemination around a primary growth, since wherever a focus of growth is situated it is in relation with the vast anastomotic network of fine vessels which lies at the periphery of the lymph-vascular system.

A Comparison between the Mode of Spread of Carcinoma and that of Melanotic Sarcoma.

The principal aim of this research has been to test the conclusions on the spread of breast carcinoma at which I had previously arrived. For if it be granted that sarcoma can obtain access to and can exist within the lymphatic vessels, its mode of spread within them must be to a certain extent determined by the same mechanical factors as in the case of carcinoma, or of an artificial injection mass.

My conclusions on the spread of breast cancer were necessarily reached by microscopic methods only, but in melanotic sarcoma a direct appeal to the eye becomes possible; and Fig. 47 strengthens my former conclusions by indicating the identity of the mode of spread of melanotic sarcoma in the parietal tissues with the mode of spread which I inferred to take place in breast cancer.

In the earlier stages the processes of dissemination are essentially identical in carcinoma and in melanotic sarcoma. Dissemination is initiated by the access of malignant cells to the fine lymphatics, followed by the centrifugal spread of permeation along the main lymphatic plexus into which the primary growth pours its lymph, and by secondary permeation of small tributaries of this plexus. Embolic invasion of the regional lymphatic glands occurs, and around this fresh focus permeation recommences. Meanwhile, invariably in melanotic sarcoma and sometimes in carcinoma, invasion of the blood-stream takes place, either by local infiltration of veins from comitant permeated lymphatics, or by malignant cells carried into the blood along the thoracic duct from invaded lymphatic glands.

When this stage is reached dissemination in melanotic sarcoma and in carcinoma respectively, develops along divergent lines. In carcinoma lymphatic permeation, aided by the escape of cancer cells into the serous cavities, usually remains to the end the main agent in producing secondary growths—a fact which appears to depend upon the almost invariable destruction of such epithelial cells as obtain access to the blood-stream.

On the other hand the mesoblastic cells of melanotic sarcoma are frequently able to thrive when lodged in a blood vessel. Thus in the later stages of melanotic sarcoma the slow process of lymphatic permeation recedes into insignificance, and the patient dies with almost universal deposits resulting from blood-embolism—an event which as a rare exception may also occur in carcinoma.

IV.—The Operative Treatment of Melanotic Sarcoma.

At present the main principle followed in operations for melanotic sarcoma is to cut wide of the growth. For digital growths amputation is usually performed. For growths upon or near the trunk the usual procedure is, I believe, to enclose the growth at some distance by a fusiform incision passing directly down to the muscles, to dissect up the tissues enclosed by this incision from the muscles which lie beneath them, and to suture the edges of the incision.

The principles upon which, in my opinion, operation for melanotic sarcoma should be based may be directly deduced from Fig. 47. This drawing may be considered to represent a radial section of the parietes starting just at the edge of the growth and passing out into the surrounding tissues.

A circular incision should be made through the skin around the tumour at what is judged by present standards to be a safe and practicable distance. This incision should just be deep enough to expose the subcutaneous fat. If necessary, two radial linear incisions extending from the circular incision may be made on opposite sides of the tumour so as to facilitate the elevation of the skin-flaps, which forms the next step. The skin, with a thin attached layer of subcutaneous fat, is

now to be separated from the deeper structures for at least two inches in all directions around the skin incision. At the extreme base of the elevated skin-flaps a ring incision down to the muscles surrounds and isolates the area of deep fascia and overlying deeper subcutaneous fat to be removed. This fascial area is next isolated centripetally from the muscles beneath, up to a line which corresponds with that of the circular skin incision. Finally the mass with the growth at its centre is removed by scooping out with the knife a circular area of the muscle subjacent to the growth. The edges of the wound are brought together as convenience dictates. The removal of the regional lymph glands is then proceeded with, and should in no case be omitted, for there can I think be no doubt that at a very early stage of the disease particles are swept to these glands by the lymph stream along the trunk lymphatic vessels.

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[243.—9/06.]