The centrifugal spread of mammary carcinoma in the parietes, and its bearings on operative treatment / by W. Sampson Handley.

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The President of the Royal College of Surgeons
With the writer's respects.

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THE CENTRIFUGAL SPREAD OF MAMMARY CARCINOMA IN THE PARIETES,

And its Bearings on Operative Treatment.

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BY

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THE CENTRIFUGAL SPREAD OF MAMMARY CARCINOMA IN THE PARIETES AND ITS BEARINGS ON OPERATIVE TREATMENT.

I.—INTRODUCTION.

In the following Paper it is proposed to consider chiefly from the clinical and macroscopical standpoint certain facts in the Pathology of Breast Cancer which hardly seem to have obtained due recognition. At the same time such modifications in operative procedure as are deducible from the pathological facts will be briefly indicated.

The necessity of scrupulously clearing out from the axilla every particle of its fat, connective tissue, and glands is so generally accepted that there is no necessity to consider this branch of the subject. Stiles has shewn that the whole breast must be removed, and that, in order to do this, the pectoral fascia and the costal part of the great pectoral muscle must be taken away. In America there is a tendency at present to extend the area of operation upwards, and to remove the glands of the posterior triangle as a matter of routine, a practice which most English surgeons regard as unnecessary.

Although the scope of the operation has been thus widened, recognition still seems to be denied (at any rate in practice) to the fact that the axillary and supra-clavicular glands, and the lymphatic routes which lead to them, are by no means the only extra-mammary structures to which comparatively early extension of the growth occurs.

There is much evidence that cancer of the breast spreads centrifugally and by continuity from its seat of origin in a way not unlike the 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 often shews 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.

II.—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 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 these nodules always appear first in the immediate neighbourhood of the primary growth. They are very rarely 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.

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.

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 about the right clavicle. In a backward direction these deposits could be

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

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.)

The other case shewed 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.)

The most extreme instance of widely disseminated skin-nodules I have found is one recorded by 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, simultaneously with the administration of arsenic and thyroid extract, the number of nodules had diminished to 78. The glands in the axillæ and groins were enlarged.

The distribution of the nodules is illustrated in two figures, one shewing the front, the other the back of the body. The figures afford very strong evidence for centrifugal spread, in

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

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.

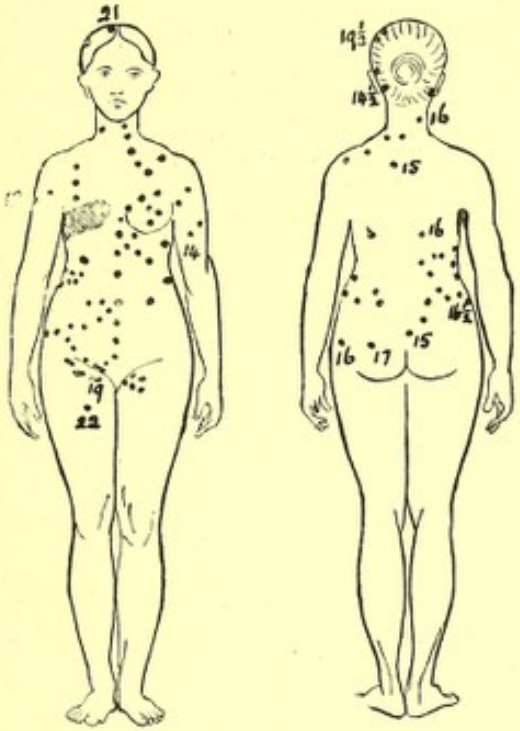

FIG. 1.—DIAGRAM SHEWING THE DISTRIBUTION OF THE SUBCUTANEOUS NODULES IN DR. ROLLESTON'S CASE.

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.

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 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 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 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 portions of the limbs.

A recent case at The Middlesex Hospital shewed a similar, but less extensive distribution of subcutaneous nodules, with the same freedom of the limbs from nodules. The distribution is therefore not accidental but characteristic. The limbs escape no doubt simply because the patient dies before the slow centrifugal spread of the growth has time to extend to them.

Cases of the kind just described 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 evidence has yet been brought forward to prove that cancer spreads *along*

the skin. Indeed, the irregular distribution of subcutaneous nodules within a regular area seems to indicate rather 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.

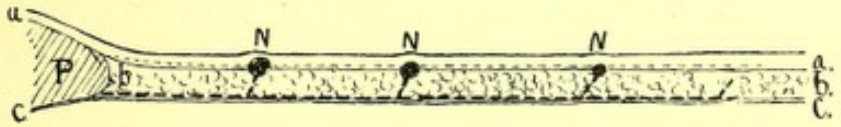

FIG. 2.—To shew that Subcutaneous Nodules do not necessarily imply the extension of growth *along* the skin.

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.

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.

Heidenhain and Stiles have shewn that breast cancer early invades the pectoral fascia, where it is found within the lymphatic vessels which lie on its surface.

The anatomical definition of the expression "pectoral fascia" is the fascia which covers the pectoralis major muscle. Lying in or upon it is a lymphatic network or plexus, giving rise to large vessels which run to the axillary glands. But the lymphatic network is in no way special to the pectoral fascia, nor bounded by its limits. At the margins of the pectoral fascia the plexiform network of lymphatic channels is continued over the abdomen, the opposite pectoral muscle, the neck, and the serratus magnus. In fact, the lymphatic plexus of the deep fascia is found as a continuous network all over the body.

There is, therefore, no anatomical obstacle to prevent cancer from growing along the meshes of the deep fascia over the whole superficial extent of the parietes, along lymphatic vessels which are indeed too small to allow the cells to be carried by the lymph stream, but which must yet offer far less resistance to the growth of cancer along them than is successfully encountered in the infiltration of a solid tissue, by way of its far smaller lymph spaces. That such growth would often have to take place against the direction of the lymph current can hardly be regarded as a valid objection to this view, considering the low intravascular pressure within the small lymphatics, the sluggishness of their stream, and the freedom of their anastomoses.

It may be objected that, if cancer of the breast extended in the fascial lymphatics beyond the limits of the pectoral fascia, its presence would have been detected by so careful an observer as Stiles. It is, therefore, necessary to emphasize the fact that Stiles' work was done exclusively on mammæ excised from the living subject at a time when wide removal of the deep fascia was not practised, so that his material allowed him to trace fascial infection only within narrow limits. Though he could only speak positively of the pectoral fascia, nevertheless, as a measure of precaution, he recommended removal also of the fascia covering the serratus magnus and the upper digitations of the obliquus externus abdominis.

Even, however, up to the present day many surgeons act as though the fascia covering the pectoralis major were the only area of the deep fascia to which mammary carcinoma may extend, and aim only at such a wide removal of it as shall ensure ablation of the whole breast and the mammary lymphatics. But the peripheral lymphatics of the mammary area

themselves anastomose with those of contiguous areas, so that invasion of the deep fascia is almost certainly bounded by a series of ever-widening circles centred on the primary growth—not by the limits of the breast, nor indeed by any anatomical boundaries. The practical importance of such a conclusion is obvious.

That cancer does tend to grow widely along the lymphatic plexuses, and to choke up their meshes, is a well-known fact, though the process has not been definitely recognized in the deep fascia. When cancer cells gain entrance to the pleural or the peritoneal cavity they may implant themselves on the serous surface, and give rise to secondary growths. Around such secondary growths a wide, somewhat opaque, roughly circular area of the serous membrane can often be seen. Close observation reveals the opacity as a fine rete of white lines, just visible to the unaided sight, and shewn microscopically to be due to the growth of cancer along the meshes of the sub-endothelial lymphatic plexus.

It is proposed to publish later a full account of some observations upon this subject.

It is not the object of the present Paper 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 shews only one plane.

1. The tissue to be examined is fixed for a few days in equal parts of commercial formalin and water.
2. A thin slice, vertical to the surface, is cut from it. 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.
4. It is washed in water and transferred to absolute alcohol.
5. When dehydrated it is transferred to cedar-wood oil, and may be preserved in this medium.

The specimen thus obtained 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 suitable 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 Fig. 3.)

(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.

Since the flat bones may be extensively cancerous without breaking, 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.

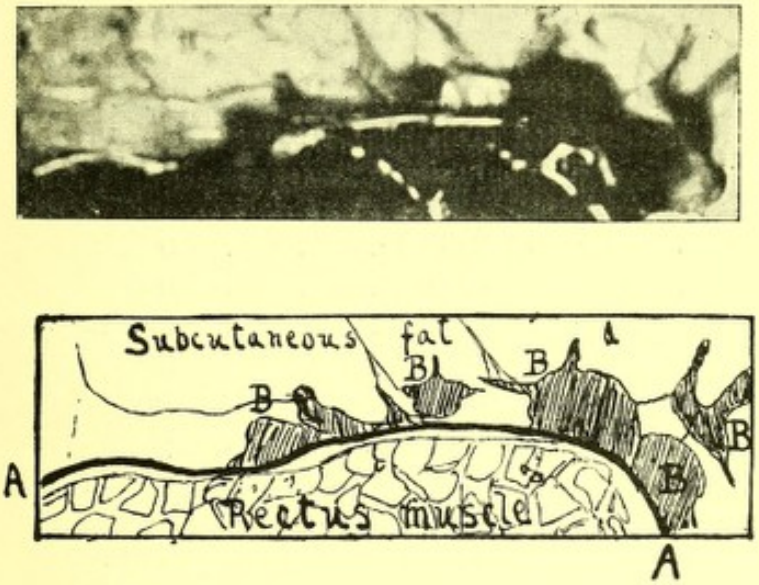

FIG. 3.—Photograph × 3, with key-diagram attached, shews a late stage of cancerous invasion of the deep fascia round a carcinoma of the breast. It represents a horizontal slice of tissue ⅛ inch thick taken from the upper part of the abdominal wall. The specimen is viewed by transmitted light. The skin 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.

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.—Shewing 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 Metastasis 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 p. 12).

† Knee ankylosed, femur affected in its whole length, with extension of growth to patella and head of tibia (see p. 21).

(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 (see Table III., p. 32), 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 (Table III., p. 34) there was 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 appears then from this list 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.

(*b*) Secondary Deposits in the Humerus.

Of the 329 cases with which this Paper deals 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 (see Table IV., p. 35).

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 always 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.

The evidence goes to shew, however, 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 absence of records of spontaneous fracture in the distal bones shews that their escape from cancerous invasion is real and not merely apparent.

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

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 shew that the conclusion is an erroneous one, and that, like subcutaneous nodules, bone deposits are 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 shew 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 shewing 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 shewing 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 shew bone deposits and the cases in which they are absent.

It is true that M. B. Schmidt* has recently shewn 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.

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.

* M. B. Schmidt, "Die Verbreitungswege der Karzinome," p. 53 (Jena, 1903).

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 Paper deals, there are two which offer apparent exceptions to this rule.

(1) In Case III., TABLE III., 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 Case IV., TABLE III., 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 shewed 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 shewn 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 shews that with this single exception (which is not in itself conclusive) the rule enunciated at the beginning of this paragraph is an absolute one. *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 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. 5, 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. 1, p. 7.)

The diagrams on p. 23 indicate 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 shewed 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 shew that both subcutaneous nodules and bone metastases result from far-reaching centri-

fugal growth of cancer in the parietes, but the question in which layer of the parietes cancer primarily spreads still remains to be settled.

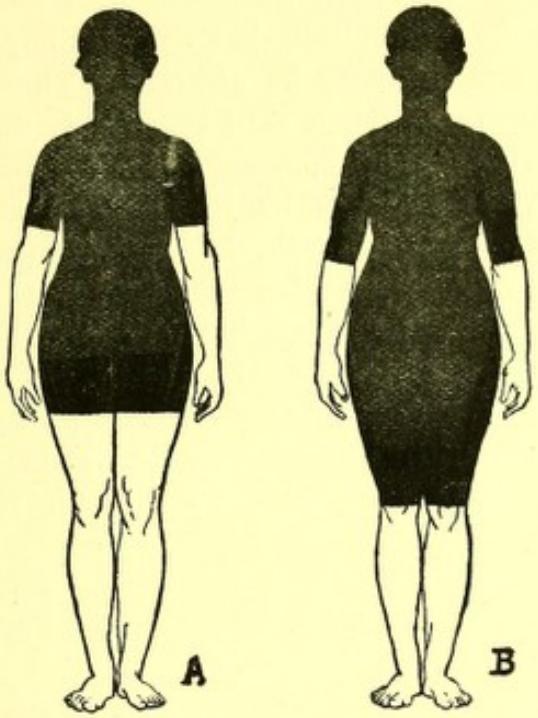

FIG. 4.—Diagrams shewing the Maximal Distribution Areas of Subcutaneous Nodules and of Metastases in Bone in Cases of Mammary Carcinoma. The black area in A is the area liable to Subcutaneous Nodules, that in B is the area within which Bone Metastases occur.

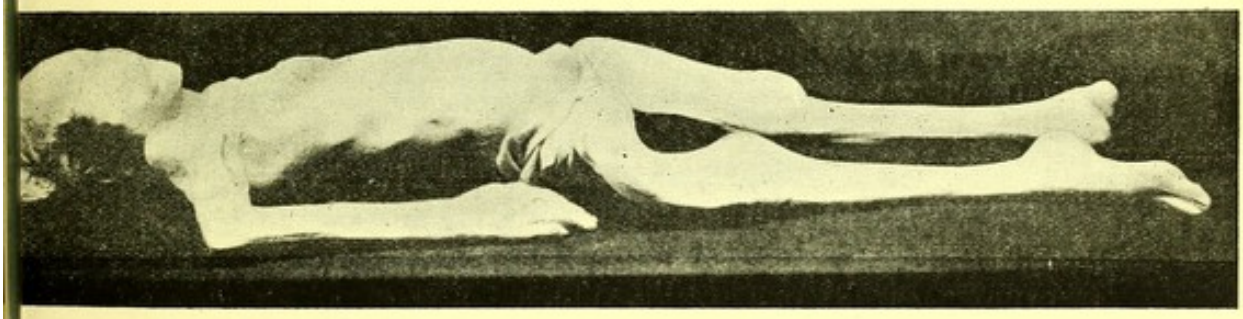

FIG. 5.—Photograph of Plaster Model, No. 673, St. Thomas's Hospital Museum, by kind permission of Mr. Shattock.—The body of a woman who died of Scirrhus of the Right Breast. The figure is inserted to illustrate the immunity of the bones distal to the knee and elbow, even in an advanced stage of Secondary Bone Cancer.

Is it possible from clinical evidence definitely to decide 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. Thus 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."

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 wrong—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 Cheyne and Halsted, who may be regarded as among the protagonists of breast surgery on this and the other side of the Atlantic.

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 be assumed therefore that the American surgeon removes rather more skin than does his English colleague.

On the other hand, Cheyne lays special stress on the undermining of the skin all round the incision. He says: ". . . . the skin incisions when made should not go straight down to

* "Lancet," March 12th, 1904.

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 region of the abdominal muscles below, and over the edge of the latissimus behind."

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 of the skin removed. His 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 summarized in the table on the following page.

This table shews 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.

TABLE II.

SHEWING 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.	21 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.**

We arrive then at the anomalous result that *the operator who removes the smaller area of skin yet has a lower percentage of skin-recurrences*, a result which goes far to prove that breast-cancer does not spread primarily in the skin, but simply here and there extends to it from the deep fascia.

In the next place these conclusions are strengthened by a study of the *site* of the skin recurrences. 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 his skin recurrences 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 shews 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.

Conclusions.

(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 the flow of lymph or blood.

(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 off-shoots (*a*) towards the surface, as subcutaneous nodules, (*b*) towards the deeper tissues, as bone (or muscle) deposits.

III.—MODIFICATIONS IN OPERATIVE PROCEDURE SUGGESTED BY THE PRECEDING CONSIDERATIONS.

(i) Removal of Skin.

Wide removal of the skin is necessary, owing to the vertical extension to it, after a time, of the growth which is spreading in the deep fascia; but removal of such an extent as interferes with subsequent approximation of the edges of the wound seems to be unnecessary, save in exceptional cases.

If after the primary operation skin nodules appear in the neighbourhood, *their significance depends on whether 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 been already 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 far from the original primary growth the case must probably be regarded as hopeless, owing to the large area of fascia involved.

(ii) Removal of the Deep Fascia.

It has been explained that the invasion of the fascial lymphatic plexus is in no way limited by the boundaries of the pectoral fascia. *The aim should, therefore, be to remove as widely as is practicable a circular area of deep fascia with its centre at the primary growth*, remembering, however, that growth extends in the fascia rather more readily in a vertical than a horizontal direction.

The use of the expression "removal of the pectoral fascia" instead of "removal of as wide an area as possible of the deep fascia," and the exclusive attention paid to the axillary glands as the channels 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. It seems to be in this direction that the scope of the operation requires extension, rather than in the direction of opening up the posterior triangle.

The following measurements shew the distance from the nipple to various points on the thorax in two patients with non-pendulous mammæ :—

	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 at least 2 inches below the tip of the ensiform cartilage.*

If the growth is in the lower and inner part of the breast the circle of infected deep fascia will encroach still more on the surface of the abdomen, and over the opposite side of the breast, and removal of the deep fascia in these directions must be carried out yet more widely.

It has often been considered sufficient, wherever the growth is situated, to remove the whole breast, its lymphatics (and therefore the pectoral fascia and part of the great pectoral muscle), the lymphatic tract running to the axilla, and the axillary contents. This aim, however imperfect, gives good results when the growth is central in the breast. But when the growth is peripheral the circle of infected fascia is almost certain, by the present mode of operating, to be intersected and partially left behind in one or other direction.

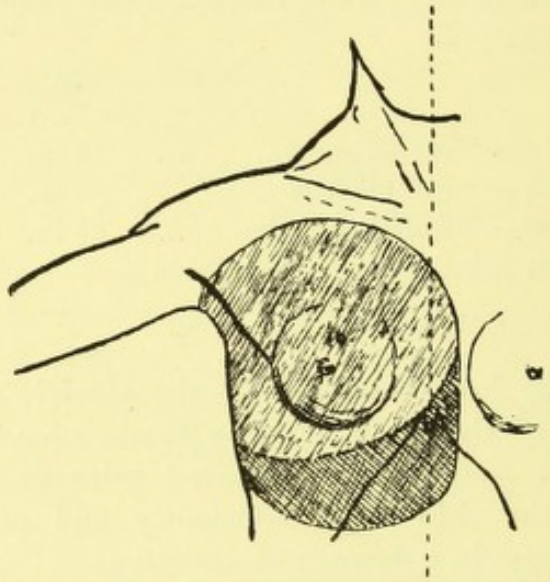

Fig. 6.—The lightly-shaded area represents the extent of deep fascia removed in the operation of excision of the breast, as at present usually performed.

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.

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.

Even when the growth is central the present operation removes far too exiguous a portion of deep fascia in a downward direction. Cheyne, who carries out ablation of the fascia as widely as any one, recommends that it should be removed below,

"over the origin of the abdominal muscles." The expression is somewhat vague, and both the rectus and the external oblique muscles are attached well above the costal margin. It is, therefore, unlikely that Cheyne's removal of fascia extends further than the costal margin, if as far; and under these circumstances it is almost certain that in some cases, while circumscribing the infected area of deep fascia above, externally and internally, his operation will intersect it below and leave a part of the infected area. Fig. 3, p. 13, which illustrates an advanced stage of infection of the fascial plexus lying on the rectus sheath, shews that this is no merely theoretical danger.

In order to obtain access to the upper part of the abdominal wall for the purpose of removing its deep fascia, the lower angle of the incision should be prolonged downwards for two or three inches over the linea alba, and the flaps undermined to a corresponding extent. Great care should be taken to remove every particle of the origin of the pectoralis major from the rectus sheath. The surface of the latter on both sides of the middle line should be most carefully cleaned—as should also the digitations of the muscular part of the external oblique—down to a horizontal line running two or even three inches below the tip of the ensiform cartilage.

TABLE III.—Secondary Deposits (or Fractures) in the Femur in 329 Cases of Mammary Carcinoma.
(Middlesex Hospital, 1872—1901.)

Case.	P.M. Number.	Site of primary growth.	Femur affected and Site.		Other bones affected.	Details.
			Right.	Left.		
I.	201, 1883	L.	Fracture 1 inch below great trochanter.	Fracture rather lower than on right side.	Right humerus fractured during the autopsy.	No cancer in connection with any of the fractured bones. Fracture of right femur repaired by a large mass of callus; not much reparative material round fractured left femur.
II.	16, 1885	R.	No details of site.	.. ..	Right humerus infiltrated and fractured.	The right femur shewed extensive infiltration of the medullary cavity, with perforation of the bone at one spot.
III.	14, 1886	L.	Infiltrated throughout, but most in its upper part; three fractures.	One inch below lesser trochanter; fracture at this point.	Left humerus, right tibia and patella (ankylosis of right knee-joint).	Right femur fractured in three places: neck, upper third, junction of middle and lower thirds. Bone distorted and in great part replaced by growth. Its outline still traceable in its lower third. Right knee ankylosed; chronic osteo-arthritis of left knee.
IV.	57, 1888	?	.. ..	Fracture 2 inches below great trochanter.	Both humeri, clavicle and three metacarpals fractured, ribs brittle.	The presence of cancer in the bones is not stated.
V.	280, 1891	L.	.. ..	Fracture just below trochanter.	Both humeri, cranial bones, spine, sternum, ribs.	Left femur fractured. Growth is stated to be present in some of the bones, but its presence in the left femur is only implied.

VI.	11, 1873	R.	Fractured at upper end.	.. ..	None.	Right femur fractured; false joint surrounding growth as large as fœtal head.
VII.	101, 1876	R.	.. ..	Just below trochanter.	None.	A large mass of osteoid cancer round the left femur, just below trochanter.
VIII.	160, 1879	R.	.. ..	Fractured in its upper part.	None.	Impacted fracture; no statement as to growth at site of fracture.
IX.	22, 1882	L.	.. ..	5¼ inches from tip of great trochanter.	None.	Spontaneous un-united fracture; no statement as to presence of growth.
X.	212, 1885	Both breasts.	Fractured at junction of shaft with great trochanter.	?	Four ribs.	Fracture of right femur at site of deposit, where there was a mass of cancer the size of a man's fist, with some calcareous deposit in it. The medulla here invaded, the cortex of the femur destroyed. Head of the bone soft and wasted, but not cancerous.
XI.	183, 1892	L.	Fractured 4 inches below head, also through neck.	Six inches below neck.	Sternum, clavicle.	New-growth found over the right great trochanter, and again about 3½ inches below this. Three inches below the lower fracture the shaft of the bone shews no new growth. No deposit of new-growth was seen about the left femur, but on removal it was found plugged with growth, reaching up ½ inch above the fracture, above which the medulla is natural.

TABLE III.—*continued.*

Case.	P.M. Number.	Site of primary growth.	Femur affected and Site.		Other bones affected.	Details.
			Right.	Left.		
XII.	135, 1893	R.	Fractured just below great trochanter.	.. ..	Sternum.	On dissecting down over the shaft of the right femur a cavity is exposed containing 10 to 20 ounces of cholocate-like fluid, within which the two rough ends of the fractured bone can be felt. The new-growth was chiefly confined to the upper fragment, involving the great trochanter, which was largely destroyed, and the shaft just below it.
XIII.	163, 1898	R.	Upper two-thirds infiltrated.	.. ..	Sternum, four ribs, frontal and parietal bones.	Upper two-thirds of shaft of right femur infiltrated; two old un-united fractures present, one ? 2 inches below the neck, the other 2½ inches lower down.
XIV.	71, 1900	R.	Fracture near upper end.	Fracture near upper end.	Frontal bone, 8th and 9th thoracic vertebræ.	Thighs much shortened and deformed by swellings at the upper end. In left femur growth invades both medullary cavity and periosteum. In the right femur the growth is less extensive, and scarcely invades the periosteum, but only the medulla of the bone. Both femora are fractured.

TABLE IV.—Secondary Deposits (or Fractures) in the Humerus in 329 Cases of Mammary Carcinoma.
(Middlesex Hospital, 1872—1901.)

Case.	P.M. Number.	Site of primary growth.	Humerus affected and Site.		Other bones affected.	Details.
			Right.	Left.		
I.	201, 1883	L.	Fracture just above elbow joint.	.. ..	Both femora.	"No cancer in connection with any of the fractured bones."
II.	16, 1885	R.	Fracture, upper two-thirds infiltrated.	.. ..	Right femur.	Right humerus fractured.
III.	14, 1886	L.	.. ..	Infiltrated throughout, but most above.	Right tibia and patella, both femora.	The left humerus, infiltrated throughout with cancer, measured on section nearly 3 inches about the level of the surgical neck, gradually tapering off to the lower end, where it was very thin, and the bone had been fractured in two places.
IV.	57, 1888	L.	Fracture lower third.	Fracture mid-shaft.	Clavicle, 3rd, 4th and 5th R. metacarpals, and left femur fractured.	No definite statement as to growth in the bones; ribs very brittle.
V.	280, 1891	L.	Fracture at Deltoid insertion, whole length infiltrated.	Fracture at Deltoid insertion.	Left femur fractured, growth on ribs, cranial bones, spine, sternum.	The right humerus in the whole of its medullary portion is occupied by pale new growth. Condition of left one not stated.

TABLE IV.—*continued.*

Case.	P.M. Number.	Site of primary growth.	Humerus affected and Site.		Other bones affected.	Details.
			Right.	Left.		
VI.	116, 1874	Both ?	Site not stated.	.. ..	Spine, right parietal and frontal bones, and basis cranii.	Right humerus broke at autopsy. Its medullary canal infiltrated by cancer.
VII.	87, 1880	L.	Fracture lower third.	.. ..	Sternum.	Right arm œdematous. Swelling most marked in its lower third, where from its mobility the bone was evidently broken. No definite statement as to presence of growth.
VIII.	162, 1899	L.	Fracture just below junction of middle and lower thirds.	.. ..	.. ..	A secondary deposit in the shaft of the right humerus.
IX.	58, 1900	R.	.. ..	(?)Fracture mid-point. (See Details.)	Parietal bones.	There is well-marked bending of the left humerus forwards, with considerable thickening of the bone near its mid-point.
X.	176, 1873	..	.. ..	.. ..	.. ..	Humerus involved by an extension of growth from the axilla. Details could not be found.