

## INVASION OF INTERNAL MAMMARY LYMPH NODES IN CARCINOMA OF THE BREAST

BY

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For the past 150 years isolated observers have been calling attention to the internal mammary lymph chain and its importance in the spread of carcinoma of the breast. No great notice has been taken of their words because they have not provided convincing proof. In 1946 it occurred to us that quantitative microscopical proof of the role of the internal mammary chain in malignant disease of the breast could be obtained by biopsy during the course of a radical mastectomy. The surprising results of this simple procedure have from time to time been published (Handley and Thackray, 1947, 1949; Handley, 1950, 1952). It is intended now to bring this published information up to date and to try to discern whether the facts are leading in the realm of treatment.

### Anatomy of the Internal Mammary Lymphatic Chain

The internal mammary lymph nodes receive lymph chiefly from the medial side of the breast and from the region of the nipple, but there is considerable overlap in the territories drained by them and by the axillary system. Afferent lymphatics from the breast reach the chain by perforating the intercostal muscles, for the most part where the anterior perforating arteries emerge. The nodes themselves lie posterior to the intercostal muscles, and Stibbe's (1918) diagrams (Figs. 1 and 2) show their general arrangement. They are inconstant both in position and in number, and there exist many very tiny nodes which are recognizable only by the microscope. The chain begins in the sixth intercostal space, where it receives lymph from the diaphragm and liver, and it ends, again inconstantly, in a node which lies behind the sternal head of the sterno-mastoid muscle and which discharges direct into the great veins. Nodes most often occur in the second, first, and third spaces in that order of frequency, and it is in these spaces that lymph from the breast is mostly discharged.

### Technique of Internal Mammary Biopsy

To remove a node for purposes of biopsy is a finicking procedure, but by no means difficult. A 1-in. (2.5-cm.) incision in the intercostal muscles, running from the edge of the sternum, midway between and parallel with the costal cartilages, will reveal extrapleural fat, imbedded in which are the lymph nodes of the chain and the internal mammary vessels; the latter usually lie about  $\frac{1}{4}$  in. (6 mm.) clear of the sternum. To detach lymph nodes requires a nice touch with two pairs of dissecting forceps, particularly as the nodes are often minute; any fatty tissue removed from a plane deep to the intercostal muscles should be sectioned as it often

contains a microscopic node. The only peril attending the procedure is laceration of the internal mammary artery, but this accident should be easy to avoid, and has not occurred in the series described here. Tears of the pleura are of no great consequence if they are recognized, and this accident has occurred to us on five occasions without untoward post-operative sequels.

### Material

The series on which internal mammary biopsy has been carried out consists of 150 cases. It is as continuous as it has been possible to make it. All patients being treated for the first time by surgery have been subjected to the biopsy. Second primary tumours occurring in the opposite breast, tumours in men, and tumours treated first by radiotherapy have been excluded. Of the 150 patients, 139 have been judged, on clinical grounds, to be operable; in 11 the biopsy was exploratory in

patients who were judged inoperable. During the time in which these numbers have been accumulating, approximately 45 additional cases have been seen in which, for one reason or another, but chiefly because of advanced spread, surgery as a primary measure has not been undertaken and no biopsy has been done; it is reasonable to suppose that, had they been included, the overall percentage of invasion of the internal mammary chain would have been higher. An analysis by quadrant, and by the numbers in which axillary metastases were found, does not differ greatly in its distribution from the large published series—for example, Truscott (1947)—and it may therefore be taken that our series is representative in these respects. One of us (R.S.H.) has done all the biopsies and the great bulk of the accompanying surgery. The latter, in the 139 operable cases, has consisted of 117 radical mastectomies, 3 Margottini operations, 3 Urban operations (see below), and 16 extended simple mastectomies.

All diagnoses are based on histological evidence, with the exception of the state of the axillary nodes in one of the clinically operable cases and in 8 of the 11 inoperable cases. All these unproved axillary nodes have been reckoned as invaded. In the earlier cases only the second intercostal space was explored.

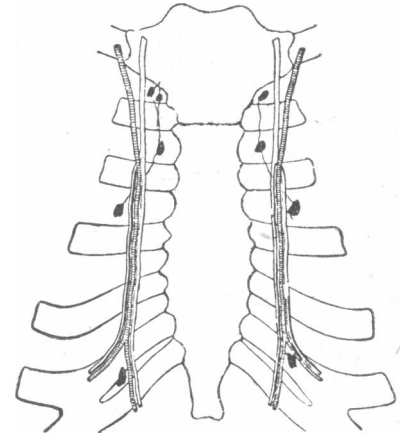


FIG. 1.—The internal mammary blood vessels and chain of lymph nodes seen from within the thorax. (After Stibbe.)

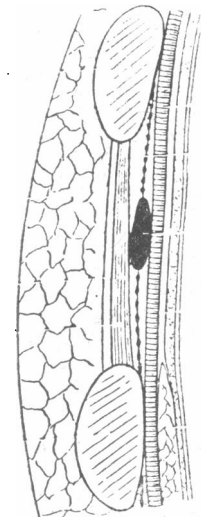


FIG. 2.—Sagittal section of the chest wall showing the pectoralis major to the left, two costal cartilages cut across, and an internal mammary lymph node lying behind the intercostal muscles. (After Stibbe.)

Later more than one space was often explored, and recently the upper three spaces have been explored as a routine. There has been no mortality.

### Results

Table I shows that 33% of the primary growths in this series had metastasized to the internal mammary chain at the time of operation. If the 61 growths in the medial half of the breast (with which are included the tumours behind

TABLE I.—Lymphatic Spread of Breast Cancer in Relation to Site of Primary Growth

	Site of Primary Growth		Total
	Inner Half of Breast	Outer Half of Breast	
All nodes free .. .. .	16	33	49
Axillary nodes only invaded .. .	12	40	52
Internal mammary nodes only invaded .. .	6	2	8
Both axillary and internal mammary nodes invaded .. .	27	14	41
Total No. of cases .. .	61	89	150

the nipple) are considered, 33 (54%) of them had metastasized to the chain, 6 of them to the chain alone, whereas only 16 of the 89 growths (18%) in the lateral half of the breast had metastasized to the chain, and 2 to the chain alone. Table II shows a further breakdown by quadrant, and it is of particular interest that 16 of the 17 growths in the region of the nipple had metastasized to lymph nodes, in 12 the internal mammary chain being invaded.

TABLE II.—Lymphatic Spread of Breast Cancer in Relation to Site of Primary Growth, by Quadrant

	Site in Breast by Quadrants					Total
	Upper Inner	Lower Inner	Central	Upper Outer	Lower Outer	
All nodes free .. .	11	4	1	28	5	49
Axillary nodes only invaded .. .	6	2	4	34	6	52
Internal mammary nodes only invaded .. .	4	0	2	2	0	8
Both axillary and internal mammary nodes invaded .. .	10	7	10	13	1	41
Total .. .	31	13	17	77	12	150

If only the tumours which had already metastasized to the axilla are considered, 41 of the 93 cases (44%) had metastasized to the internal mammary chain. Of the 39 cases in which a tumour in the inner half of the breast had metastasized to the axilla, the internal mammary chain was invaded in 27 (69%). Even with tumours in the outer half of the breast, if the axilla was invaded 14 of the 54 cases (26%) had internal mammary deposits.

An attempt was made to see whether the degree of anatomical invasion of the axilla bore any relation to the frequency of internal mammary deposits. There were 146 cases in which the data enabled a rough estimate to be made of the anatomical degree of axillary involvement, and four degrees, from 0 to 3, were somewhat arbitrarily fixed by the clinical state of the patient, the number of invaded lymph nodes sectioned, and whether or not the apical axillary nodes were involved.

Table III gives the results, and it shows what one might expect—namely, that the greater the degree of axillary

TABLE III.—Relation of Degree of Axillary Involvement to Internal Mammary Invasion (146 Cases)

Extent of Axillary Invasion	No. of Cases	Cases with Internal Mammary Invasion
0 (free) .. .	57	8 (14%)
1 (light) .. .	23	6 (26%)
2 (moderate) .. .	32	12 (37%)
3 (heavy) .. .	34	22 (65%)

involvement the more likely is it that the internal mammary chain will be invaded—but it disposes of the argument that only after the axillary lymphatics are completely choked is the chain invaded.

To compare the results of different workers in the field of mammary cancer, some index of the extent of the disease in individual cases is needed. A system of staging has therefore been evolved, based for deciding treatment on the clinical findings and for scientific purposes on pathological and radiological evidence. We have staged our cases into three groups according to whether the carcinoma was confined to the breast (stage I), had not spread beyond the limits of the standard radical mastectomy (stage II), or had spread beyond those limits (stage III). We have thus placed a patient with internal mammary deposits in stage III. No other series, however, has been staged in the light of internal mammary biopsy, and it seems that this may account for the very small differences in the results of treatment which many have found between stages II and III. Yet, without knowledge of the state of the internal mammary nodes, a stage III case must often be classified as stage II and occasionally as stage I.

Table IV shows the effect of internal mammary biopsy on staging. It demonstrates the well-known though appalling inaccuracy of clinical staging. The last two columns of the table reflect the effect of the biopsy procedure on the

TABLE IV.—Effect of Internal Mammary Biopsy on Staging

	Clinical	Pathological	
		Ignoring Internal Mammary Findings	In Light of Internal Mammary Findings
Stage I .. .	79	57	49
.. II .. .	63	85	52
.. III .. .	8	8	49

pathological staging. Whereas stage I is not much affected, there is a "landslide" between stages II and III, the 85 stage II cases being reduced by the biopsy findings to a mere 52, and the stage III cases being increased from 8 to 49.

In this series 75 patients had their biopsies three or more years ago. The results in terms of three-year survival are shown in Table V. Three-quarters of the patients with metastases only in the axilla are alive, whereas only one-third of those with both axillary and internal mammary metastases are still living.

TABLE V.—Three-year Survival (75 Cases)

	Total No. of Cases	No. Alive
All nodes free .. .	24	22 (all well)
Axillary nodes only invaded .. .	24	18 (5 with recurrence)
Internal mammary nodes only invaded .. .	4	4 (all well)
Both internal mammary and axillary nodes invaded .. .	23	8 (3 with recurrence)

The result has been good in those in whom the lymph nodes were not invaded. But one striking and apparently contradictory result is that all the four patients in whom the internal mammary chain alone was invaded are alive and well, a finding which does not accord with the importance which we would give to invasion of the internal mammary chain; it may be that what was intended only as a biopsy was, by lucky chance, an effective therapy in an early internal mammary invasion.

### Discussion

It has long been known that carcinoma of the breast may spread by way of the internal mammary chain, but this has been assumed to be a late manifestation of the disease and has not been taken into account in planning the primary treatment. What the present investigation demonstrates is the frequency with which the chain is involved in cases

operated upon as soon as the diagnosis is made, especially when the primary tumour is in the inner part of the breast. About a third of the operable cases have been shown to have deposits in their internal mammary glands, the tumour being therefore beyond the reach of the standard radical mastectomy. Since other workers, stimulated by our original publication, have repeated the investigation, sometimes on larger series than our own and with substantially the same findings, the frequency and importance of internal mammary spread can be taken as satisfactorily demonstrated (Dahl-Iversen, 1951; Gardner *et al.*, 1951; Haagen- sen, 1952, personal communication; Margottini, 1952; Moguilevsky, 1952, personal communication; Redon and Lacour, 1952; Wangensteen, 1952, personal communication). The discussion will therefore be confined to a short consideration of the effect of this finding on the treatment of the disease.

It has been suggested that, once the internal mammary chain has been invaded, the patient's situation is irremediable, because tumour cells must then have spread beyond therapeutic reach along this or other pathways. Though it is not possible at the present time to disprove this view, only the darkest pessimist would decline the challenge which invasion of the internal mammary chain presents. Halsted, when he introduced radical mastectomy, had never seen a case of carcinoma of the breast cured, and he did not know what the result of his new operation would be. To devise methods for treating the internal mammary deposits is therefore a very proper experiment, but one which it will need some years to evaluate.

Surgical excision and radiotherapy are the only potentially curative methods which exist at present for attacking the internal mammary chain. It is natural that radiotherapy should have been tried first, because until recently wounds of the pleura were regarded by surgeons with dread, and even now no surgeon would wish to add further mutilation to radical mastectomy unless he had compelling reasons for doing so. The first attempt to irradiate the internal mammary chain as a routine was Sampson Handley's (1927) method of burying radium tubes in the intercostal spaces at the time of radical mastectomy. The results were not encouraging, partly perhaps because the intensity of irradiation round a radium needle falls very rapidly and uniform carcinolytic dosage is not therefore achieved along the whole chain, and partly because it is technically difficult to insert radium needles in the very narrow anterior ends of the lower spaces.

In the mistaken belief that surgical excision of the chain was not feasible, we decided in 1947 to treat the chain in our series by deep x-ray therapy, and we enlisted Professor B. W. Windeyer's willing co-operation. It is, however, difficult to deliver an adequate dose of irradiation to the chain without damaging adjacent normal structures, and the only evidence we have so far obtained is not particularly reassuring. This evidence is the three-year results in our first 75 patients, quoted already, who were treated by radical mastectomy and, if any lymph node was invaded, by deep x-ray therapy; and the results of internal mammary biopsies done on nine cases (not included in the main series) in which radiotherapy was the first line of attack on the primary tumour. Six of these nine cases were regarded as inoperable when first seen, and in five cases carcinoma cells of viable appearance were seen in the post-irradiation biopsy. Three were earlier operable cases, and in all the biopsy was negative. These results have led Professor Windeyer to alter his technique in order to irradiate the chain more intensively, and the results of this change will be awaited with interest.

This evidence is not so satisfactory as to make experimental extensions of the standard radical mastectomy unjustifiable. Margottini and Bucalossi (1948) were the first to add excision of the chain as a routine, which they did by removal of the second and third costal cartilages, thereby gaining access to the upper part of the chain without deliberately entering the pleura. The chief theoretical objection to

their procedure is that it is not a monobloc operation. Wangensteen (1950) has described his super-radical mastectomy, which combines a supraclavicular dissection with a median sternotomy and removal of lymph nodes not only in both internal mammary chains but also further inside the chest. He has not yet published his results, but the mortality of this operation seems to be considerable, and it also suffers from the theoretical disadvantage that it is not a monobloc procedure. Urban (1952) has published a technique which appeals to us as the most likely to yield better results, because by a deliberate opening of the pleura he achieves excision of the upper part of the internal mammary chain in one piece with the breast and axillary tissue, an operation which he has done 103 times with one death. All such extensions of surgical treatment, however low their mortality in the hands of their architects, would, if generally adopted, raise the immediate death rate of breast-cancer surgery. Until their value has been proved, there is no reason for those without a prime interest in carcinoma of the breast to abandon accepted methods.

The problem of carcinoma of the breast holds many imponderable factors. We cannot yet assess with much accuracy the malignancy of tumours, and we know almost nothing about host resistance to their spread. Until the biochemistry of tumour growth and host-resistance is better understood we can only grope by mechanical means along therapeutic paths which are dimly indicated by morbid histology and judge by the slow criterion of the end-result whether the technique we follow is better (or worse) than its predecessor.

### Summary

Biopsy of the internal mammary lymph chain at operation was carried out in 139 patients with "operable" carcinoma of the breast. In 41 cases (29%) invasion of the chain by carcinoma was found on histological examination. Of a further 11 "inoperable" cases, 8 showed invasion of the chain.

Invasion of the chain was three times as frequent when the primary growth was situated in the inner half of the breast as when it was in the outer half.

Biopsies of the internal mammary chain in patients with primary growths in the inner half of the breast and metastasis in the axillary lymph nodes showed invasion in over two-thirds of the cases.

The internal mammary chain was invaded in eight cases without involvement of the axilla.

The relation of the biopsy procedure to staging and three-year survival is studied.

Some tentative reflections on the therapeutic challenge presented by these findings are offered.

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