

## BREAST CANCER: ASPECTS OF LOCAL RECURRENCE\*

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'No matter how early a case of cancer or how thorough the treatment, no patient is free from the possibility of recurrence until death ensues from some other cause.'<sup>1</sup> This fact has been known for many years, and it applies particularly to breast cancer. Why recurrences occur 20-30 years after initial operation is debatable, but an interesting observation noted by Sir Gordon Gordon-Taylor<sup>2</sup> is that these recurrences often seem to be preceded by some surgical operation for an independent condition or after a chance intercurrent illness.

By local recurrence is meant the reappearance of cancer, in the area of the operative field or close to it, at any time after the removal of the primary tumour. These recurrences are to be differentiated from regional metastases, so-called 'new' cancers in the other breast, and involvement of supraclavicular or mediastinal lymph nodes. The diagnosis may have to be confirmed by biopsy to differentiate the lesions from 'pseudo recurrences'.<sup>3</sup>

At Groote Schuur Hospital, Cape Town, we saw and treated 67 female patients with recurrent breast cancer during the 6 years, 1954-1959. The original treatment of the breast cancer in each case is shown in Table I. During the 6 years 823 patients with breast cancer were

TABLE I. ORIGINAL TREATMENT OF PATIENTS WITH RECURRENT BREAST CANCER

Treatment	No.
Radical mastectomy and postoperative DXR	37
Pre-operative DXR and simple mastectomy	12
Simple mastectomy and postoperative DXR	7
Radical mastectomy only	5
Simple mastectomy only	3
Pre-operative DXR and radical mastectomy	2
Local excision, DXR and androgens	1
Total	67

DXR= Deep-X-ray therapy.

seen at the hospital on whom a total of 369 radical and 71 simple mastectomies were performed. In the overwhelming majority of patients the surgical treatment was combined with the application of deep-X-ray therapy.

Table II shows the incidence of recurrent cancer as seen at Groote Schuur Hospital. The left-hand column gives the figures for those who were treated by surgery as well as by radiotherapy at the hospital, and compares them with those of patients referred to Groote Schuur Hospital from outlying hospitals for radiotherapy before or after (usually after) surgical ablation, or for hormone therapy. Note that 3 patients who had originally been reported as having tumour-free axillae, and 19 whose axillary lymph nodes had shown signs of invasion, developed recurrences. I shall refer to the 3 patients with no lymph-node involvement again. The higher incidence after simple mastectomy is undoubtedly due to the more advanced nature of the growths in these cases.

\* Based on a paper delivered at the Second Congress of the Association of Surgeons of South Africa (M.A.S.A.), Durban, 17-20 September 1960.

TABLE II. INCIDENCE OF LOCAL RECURRENCE AT GROOTE SCHUUR HOSPITAL, 1954-1959\*

Operation	GSH patients	Referred to GSH for DXR; surgical treatment elsewhere
Radical mastectomy:		
Operation - no nodes	103	
Recurrences - no nodes	3	
Incidence	2.9%	
Operation - with nodes	107	
Recurrences - with nodes	19	
Incidence	17.7%	
Total:		
Radical mastectomies	210	159
Recurrences	22	22
Incidence	10.5%	13.8%
Simple mastectomy:		
Total	47	24
Recurrences	15	7
Incidence	32%	29.1%
Total number of operations (radical and simple mastectomies)	257	183
Total recurrences	37	29
Incidence	14.4%	15.3%

GSH= Groote Schuur Hospital. DXR= Deep-X-ray therapy.

\* One patient who had a local excision of a carcinoma is not included in this table.

## TREATMENT AND PROGNOSIS OF PATIENTS WITH RECURRENCES

The recurrences often appeared insignificant: small lumps, coloured red or brown, usually multiple, painless and not tender. Many were frankly ulcerating.

*Time of Onset after Original Treatment*

Of the patients with local recurrences, 62% developed nodules within 1 year, and 90% within 3 years. This is in accordance with other reports.<sup>3</sup> We have records of recurrences appearing 10 and 12 years after treatment, but such patients do not fall within the scope of this follow-up.

*Associated Secondary Manifestations*

The incidence of patients developing secondary manifestations in our series, apart from local recurrences, was as follows: nodules in the opposite breast, 22%; skeletal metastases, 24%; intra-abdominal metastases, 11%; and intrathoracic metastases, including lung lesions and pleural effusions, 28%. In 15% of our cases there were only local skin nodules.

The commonest lesions were those found in the thorax, usually in the form of a pleural effusion. Many had skeletal metastases, and the skin nodules usually occurred before the bone secondaries were apparent, but sometimes they were discovered simultaneously. In 15% of the patients the lesions were localized to the original breast area and in a further 22% the nodules had also spread to involve the contralateral chest wall.

*Treatment of the Skin Nodules*

In many instances the skin nodules were the least serious of the secondary manifestations and treatment was then mainly directed at the other lesions. Where deep-X-ray

therapy had not previously been given, the treatment was often easy and most effective. Radiotherapy then cleared the chest wall in a most gratifying manner. These patients tended to do well, and it is possible that they would not have developed the recurrences had radiotherapy been given at the time of the original surgical treatment.<sup>4</sup>

The treatment of those recurrences which appeared after both surgery and radiotherapy proved extremely difficult. Further radiotherapy often failed to stem the progression. Local excision was feasible on only 2 occasions because of the usual multiplicity of the lesions, and in 1 instance it was followed by the rapid appearance of other nodules all over the chest wall. In no case did we resort to forequarter amputation.<sup>5</sup> In the majority of patients hormonal therapy was given (Table III). There were some encouraging results after oophorectomy in the younger age

TABLE III. HORMONAL TREATMENT OF PATIENTS WITH SKIN NODULES

Treatment	No.	Objective response	Subjective response	Unchanged	Worse
Oophorectomy	18	6	2	10	—
Testosterone	24	3	4	16	1
Oestrogens	11	—	4	7	—
Ovarian irradiation	1	—	—	1	—
Adrenalectomy	3	—	—	3	—
Hypophysectomy	3	—	—	3	—

group; unfortunately the response was usually short-lived and recrudescence of the lesions became apparent within 12-18 months. All these patients are now dead from cancer and in none did the local lesions completely vanish. Testosterone and oestrogen therapy for local recurrences proved disappointing.

#### Follow-up Studies

Of the patients treated, 11 are alive and free from carcinoma. All had been successfully treated with deep-X-ray therapy, and in 1 the lesion had also been excised. A typical example is Mrs. I. H. (57/02338), 45 years, who had had a simple mastectomy after deep-X-ray therapy for an attached lump, 3-4 cm. in size, in the lower and outer quadrant of the left breast, with lymph nodes palpable in

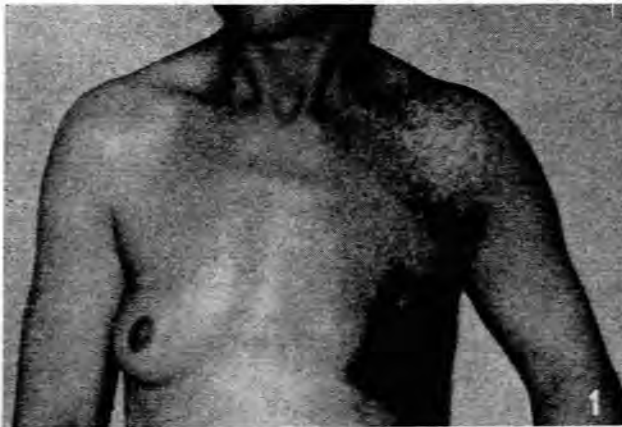


Fig. 1. See text.

the apex of the axilla. The skin nodule seen in Fig. 1 appeared seven months later and it responded well to treatment by contact radiotherapy.



Fig. 2. See text.

Ten patients are alive, but with local disease present and progressing. In 2, the lesions are extending slowly over the years, e.g. Mrs. I. S. (153520), aged 67 years. Local nodules have been present since 1954 and they are extending slowly but surely although she has been given radiotherapy, oestrogens, androgens and 'thio-tepa'. Fig. 2 shows the nodules in 1957, while Fig. 3 shows them in 1959.

The remaining 46 patients have died, still with their local disease, and in many cases with distant secondaries as well. The overall mortality rate in our series is as follows: 1 year after treatment, 40% were dead; 2 years after treatment, 60% were dead; and 3 years after treatment, 72% were dead. This reveals the alarmingly poor prognosis of these patients, a prognosis equivalent to any of the most advanced or 'virulent' forms of cancer. Our findings agree with those of Conway and Neronara,<sup>6</sup> who stated that the onset of local recurrences was a grave prognostic sign and almost all the patients in whom they occurred were dead within 5 years. Some believe that the cancer-free period before the onset of the recurrences may parallel the survival period,<sup>7</sup> but this is denied by others.<sup>8</sup>

It has been stated that the recurrence index is higher in patients treated by simple mastectomy compared with those undergoing radical mastectomy.<sup>9</sup> If this is true, and if the outlook is so bad for those with recurrent breast



Fig. 3. See text.

cancer, then, surely, a good case can be made for the radical operation.

#### FACTORS WHICH PLAY A PART IN THE PRODUCTION OF RECURRENCES

In this series the races, age groups and sexes were not factors. During the period under review only 10 male patients were treated, and this accounts for the absence of males in our series.

#### The Pathology of the Original Lesion

An attempt was made to correlate the histopathological appearance with the clinical progression of these and other patients with breast cancer. This was done by trying to grade them according to the method described by Bloom and Richardson,<sup>10</sup> by noting tubular formation, nuclear pleomorphism, numbers of mitotic figures, and the appearance of hyperchromatic nuclei. Dr. Martin Sacks of the Department of Pathology, University of Cape Town, compared the histology of patients who had recovered exceedingly well after surgical treatment with those who had died or developed extensive recurrences within 1 year of surgical treatment.

The difficulty of grading tumours soon became obvious, and the correlation with clinical progression was impossible in many cases. The appearance of the tumour often varied from slide to slide, and from field to field on the same

slide, and it was difficult to know which part of the slide to accept for grading purposes. It was also often difficult to duplicate the grading from day to day and, because of the human factor, cases of moderate malignancy could easily be graded on one day as severely malignant, and on another as mildly malignant. No uniform pathological appearance correlated with clinical follow up, and it seemed reasonable to assume that the pathology, as seen histologically, was probably not an important factor in determining the onset of recurrences.

In 2 of our patients the recurrences may have been, at least, partly due to the nature of the pathology in that they were both cases of sarcoma of the breast. In a 30-year-old African female (A.M., 59/20192), a horrible



Fig. 4. See text.

recurrence grew out only 1 month after local mastectomy (Fig. 4). She died soon after this from her disease, a highly cellular spindle-celled sarcoma.

#### Influence of Lymph-node or Lymphatic Invasion

This includes intercostal lymph vessels, internal mammary nodes, and axillary lymphatics and nodes, and will be discussed under 4 headings.

##### 1. Axillary Nodal Involvement in Our Series

Clinical and pathological examination revealed axillary node invasion in all save 3 of our patients. However, the subsequent progress in these 3 cases, described hereunder, suggests that they, too, had lymphatic involvement at the time of their original treatment.

(a) S. le G. (55/12639). Two years after radical mastectomy she developed a large supraclavicular node on the ipsilateral side, as well as skin recurrences. Four years after operation she had ascites and hepatic metastases. In spite of a negative pathology report, I feel there must have been lymphatic invasion at the time of the original operation to account for the invaded supraclavicular node arising after the mastectomy.

(b) C. M. (56/01422), and (c) R. M. (138922). Both



these patients developed skin recurrences after radical mastectomy. Both their lesions were in the upper and inner quadrants, and in spite of a negative axillary-node report, may well have had internal mammary lymphatic invasion. This seems all the more likely because both developed recurrences in the parasternal area.

## 2. The Site of the Recurrent Nodules

The nodules tended to congregate around the original scar and in the more advanced cases the whole scar became completely replaced by carcinoma. Closer examination revealed a clustering of the nodules in certain dis-



Fig. 5. This demonstrates the numbers of patients in this series with lesions concentrated at the sites shown. For purposes of clarity all lesions are shown as occurring on the right side. In some patients the lesions occurred in more than one area.

tinct areas, namely in the upper and outer quadrants extending towards the axilla, and also in the parasternal regions (Fig. 5). They seemed to be more numerous in sites where lymphatics were mainly concentrated or possibly more exposed, i.e. in the regions of the axillary and internal mammary lymphatics and lymph nodes. This is well demonstrated in Figs. 6 and 7. Fig. 6 shows the local mastectomy scar of M.M. (55/792) in 1957. Fig. 7 shows the recurrence in 1958, which occurred towards the axilla where lymphatics could be incriminated, and not in very close association with the operation scar. Fig. 8 shows the chest wall of S.M. (57/17228), an example of a recurrence in the parasternal region following a simple mastectomy for a large central growth.

It was not uncommon to find recurrences confined to these 2 regions — towards the axilla and in the parasternal area — in one and the same patient. The tendency to congregate in these regions, I feel, lends support to the theory of lymphatic invasion at the time of the original treat-

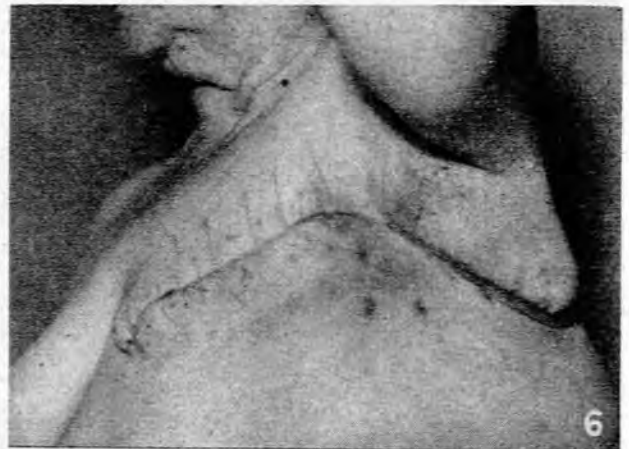


Fig. 6. 25 July 1957. Local mastectomy for large upper and outer quadrant carcinoma attached to skin and deep fascia. Postoperative radiotherapy given.

Fig. 7. Same patient as in Fig. 6, 16 September 1958. Gross axillary recurrence extending to the front of shoulder. The patient died soon after this.



Fig. 8. See text.

TABLE IV. LOCAL RECURRENCES FOLLOWING RADICAL MASTECTOMY IN VARIOUS SERIES

Recurrences	Roosevelt Hosp. <sup>12</sup>	Henry Ford Hosp. <sup>12</sup>	Johns Hopkins Hosp. <sup>12</sup>	Hopkins Hosp. <sup>12</sup>	Haagensen <sup>11</sup>	Presbyterian Hosp. <sup>11</sup>	Mayo Clinic* 1945-1954	Parsons <sup>1a</sup>
	Plastic closure	Plastic closure	Plastic closure + skin graft	Plastic closure	Thiersch graft	Plastic closure + skin graft	Closure of skin	Plastic closure, limited skin excision
	%	%	%	%	%	%	%	%
Limited to breast	10.8	5.5	6.1	—	—	4.4	10	—
Axilla involved	31.5	27	20.8	—	—	24.4	30	—
All cases	22.7	10.7	15.4	39.7	30.1	11	23	8

ment. Occasionally recurrences were seen at sites far removed from the breast area, i.e. over the neck, back, face, and even over the eyelids. We have seen 2 such patients, and in both instances these reacted very favourably, though temporarily, to oophorectomy. There is no reason why lymphatic permeation could not be incriminated, even in these widespread nodules.

### 3. Influence of Invaded Lymph Nodes on Incidence of Recurrence

It has been shown that the higher the incidence of nodal invasion the higher the incidence of recurrence.<sup>11</sup> The likelihood of recurrences also increases when the lymph nodes are more obviously invaded. This is shown in Table IV, which summarizes recurrence rates as found in the literature, and emphasizes the point that when lymph nodes are frankly invaded, the incidence of recurrence is 3-6 times higher.<sup>8, 11-13</sup> Table IV also shows that various types of skin closure bear no relation to the recurrence rate.

illustrated in Fig. 9. In this series 55% of the patients had oedema of the breast; in some it was frankly dependant and in others there was only a little over the tumour itself. Not only was the incidence of recurrence high in the presence of *peau d'orange* but, in the cases we saw, the nodules usually arose very soon after operation, sometimes as early as 3 months.

From the 4 points discussed it is reasonable to conclude that lymphatic invasion at the time of the original treatment is the most important single factor that determines the possibility of recurrence.

### Cancer Left Behind in the Subcutaneous Tissues or in the Skin Edges

From the surgical point of view the problem of cancer left behind in the subcutaneous tissues or in the skin edges is often mentioned and stressed. This may occur by leaving skin flaps which are too thick, or by not taking away enough skin at the time of the original operation—usually during the radical mastectomy.

#### 1. Leaving Skin Flaps which Are too Thick

Very thin skin flaps are virtual full thickness skin grafts, with an embarrassed blood supply, particularly if there should be any tension. This leads to a high incidence of sloughing, prolonged periods of dressings and further grafting operations. On the other hand thick skin flaps heal much better and sooner, and radiotherapy can be applied earlier, and probably in larger doses.

If one has to depend on the removal of tissue about 1 millimetre thick to cure a cancer patient, then I believe the lesion is already incurable. It is difficult to understand how the removal of a little superficial fascia really can make the difference between cure and recurrence in the operable case. I believe that if a thick skin flap cannot be safely left behind, then the case is incurable. Auchinloss<sup>14</sup> has shown that in spite of meticulous cutting of very thin skin flaps, recurrences do occur too frequently.

#### 2. Leaving Skin Flaps which Are too Large

Table IV shows the influence on the incidence of recurrences of the various types of skin closures, i.e. wide excisions with skin grafts on the one hand, and plastic closures on the other, and it shows that this factor is not a significant one. This is confirmed by Handley,<sup>15</sup> and, interestingly enough, even by Haagensen.<sup>11</sup>

Haagensen, a most meticulous surgeon, who removes skin very widely (at least 7 cm. from the tumour edge



Fig. 9. J.G., aged 56 years. She had an upper and outer quadrant carcinoma with dependent *peau d'orange*. Seven months after radical mastectomy the recurrences appeared. This picture was taken 3 years after operation. The patient died soon afterwards from gross local disease.

### 4. Influence of Oedema of the Breast

*Peau d'orange* indicates widespread lymphatic permeation, and it is therefore not surprising that some of our worst recurrences occurred after radical mastectomy in those patients who had evidence of this oedema, e.g. J.G. (57/12753), whose extensive local recurrence is well

finds that even in his expert hands the recurrence rate of his patients is high. After radical mastectomy, where lymph nodes are invaded, his recurrence rate is no less than 24%. Haagensen blames his criteria for operability; this is surprising, since his criteria for radical mastectomy are extremely strict, and he removes skin very widely—even so, his recurrence rate is still high. At Groote Schuur Hospital we have 3 patients who for various reasons had a simple excision of proved breast carcinoma 2–7 years ago and are still without skin recurrences. Their skin excision could not have been more limited.

#### CONCLUSIONS

Let me hasten to add that I am not advocating any change in the treatment of breast cancer, nor am I advocating less skin removal at the radical mastectomy operation; neither do I suggest limiting the scope of this operation. What I am trying to show is that, when dealing with a clinically operable breast cancer, what matters is the problem of lymphatic invasion. If the lymphatics are not invaded, it probably does not matter whether one takes thick or thin, wide or limited skin flaps—the outcome will always be so much the better. On the other hand, should the lymphatics be invaded, the nodules may well arise in spite of drastic attempts at radical surgery.

It has been stated that 'if persistent disease is shown by local recurrence it must be concluded that the operative procedure was inadequate'.<sup>2</sup> This is correct, but it is also correct to add that the patient should probably not have been operated on at all, since the most extensive surgical procedure possible would not have prevented the manifestations of recurrent disease in such cases.

There are many other factors in the production of recurrences, e.g. the problem of contamination by biopsy and the effect of radiotherapy used to prevent recurrences. These are beyond the scope of this paper.

If lymphatic invasion is so important in this problem, then it becomes all the more important to do the radical operations on early cases. Because selection is always a purely clinical matter, more advanced lesions, unsuspected by the surgeon, will be included in the operable series, accounting for the persistence in the incidence of recurrences. Haagensen has stated that to date no way has been found of eradicating this complication.

The results in this series indicate that in the vast majority of cases local recurrence in breast cancer is a sign that lymphatic invasion has taken place, with the

consequent probability of widespread metastases apart from the local recurrences. These recurrences, therefore, hold a very grave prognosis.

I feel it appropriate to end by paraphrasing J. Hadfield's<sup>16</sup> quotation of Celsus: There is no so great danger of breast cancer unless it be irritated by the imprudence of the surgeon.

#### SUMMARY

During the years 1954–1959, 67 patients with recurrent breast cancer were seen and treated at Groote Schuur Hospital. The majority of these also had distant metastases. Many of them were temporarily improved by oophorectomy. The mortality rate revealed the serious prognosis of these patients. It was felt that the most important single factor in determining the onset of the recurrences, was lymphatic permeation at the time of the original treatment of the breast cancer. This factor determined the persistence of the disease in spite of attempts at eradication by radical surgery. Included under the heading of radical surgery were such manoeuvres as the cutting of very thin skin flaps and the excision of wide areas of skin around the tumour.

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