

VIEWS ON THE TREATMENT OF CARCINOMA OF THE BREAST *

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My remarks in this paper are addressed, in the first place, to the average general surgeon—amongst whom I class myself—practising under present South African conditions. Because we are not mammary specialists, we cannot depend on our personal experiences alone, and must, to a certain extent, be guided by the collective experience of surgeons working in the more populous areas of the world. At the same time we must realize the particular conditions under which we practise, and adjust our treatment to suit them.

Unfortunately the masses of statistics with which the surgeon is confronted, with all their contradictions—probably more apparent than real—are difficult to digest. They have added to the headaches of the surgeon when, in a given patient, he has to decide on the 'best' method of approach. Moreover, his confidence has been somewhat shaken by Harrison's recently published statistics,¹ according to which it is *not possible to prove that the final mortality rate from carcinoma of the breast is actually influenced by treatment at all.*

I am first going to discuss the problem from a theoretical point of view; and then I shall outline an approach which is practicable and, I trust, in keeping with present knowledge. I do not believe that the bulk of surgeons practising in 1958 should adopt procedures which, if acceptable at all, can only become generally acceptable in, say, 1968. Of course, it is a completely different matter for a few fortunate individuals who have the material and all the facilities for clinical experimentation and control. Generally speaking, it is wiser to wait until we can be guided by the results obtained in large and comparable series of cases observed over long periods in the same institution. As far as I can judge, at the present time there is as little cause for over-optimism about the newer methods of treatment as there is for undue pessimism about the older methods when, that is, we consider the problem merely from the point of view of the survival rate. In the field of palliative treatment, however, undoubted advances have been made.

THEORETICAL CONSIDERATIONS

1. At its inception carcinoma of the breast is *not* a generalized disease. I make no apologies for this statement, because in my opinion it is a timely one. There is a time when carcinoma

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of the breast is a local disease, and therefore curable. Neither has it been proved to be a widely disseminated disease in a significant percentage of patients at the time of its first diagnosis. For a certain period, therefore—and this may be only a few months or several years—the disease is sufficiently localized to enable us to eradicate it by treatment applied merely to those tissues which the surgeon is able to excise with a minimum of danger. These tissues are the mammary organ and the axillary lymph nodes (I discuss other lymph nodes below).

2. An immunity response to the invasion by malignant disease is a theoretical consideration which cannot be disregarded. A natural cure has been reported in many cases of proved carcinoma of the breast. In other cases cures have followed on treatment which certainly could not have eradicated all cancerous tissue. Malignant cells have been found to enter the bloodstream at a relatively early stage of the disease;² but not all patients so affected succumb to the disease. Somehow and somewhere these cells are destroyed. Destruction most likely depends on the presence of antibodies which develop in the blood and other body fluids and tissue cells. There may even be a hormonal participation in this immunity response. In this respect it is well to remember that the cancerous process is almost certainly an irritating one to the tissues of the host. How can we otherwise explain the development of so much fibrous tissue? The laying down of collagen fibres is an important defensive mechanism which is found characteristically in the so-called atrophic scirrhous carcinoma. Malignant cells spilt at operation may become encapsulated by fibrous tissue and in this way be put out of action. In summary I emphasize that on at least two theoretical grounds it would be a mistake to accept the pessimistic view that no matter what we do, or omit to do, the end result will be just the same.

A recent publication by Berkson *et al.*³ was very welcome, because it showed us the other side of the picture. They reviewed the results obtained in nearly 10,000 patients treated at the Mayo Clinic over a period of 45 years from 1910 to 1954. I want to refer particularly to the 660 patients who received treatment in the years 1910 to 1915, i.e. over 40 years ago, and of whom an up-to-date record is available. Ten years after treatment 38.1 out of every 100 of these patients were still alive, as compared with 80.3 out of every

100 of the normal population. On this basis some 47% of cases of breast cancer, whether early or advanced, might be alive 10 years after their treatment. In patients whose axillary nodes were free from metastases at the time of operation, the 10-year survival rate was 75%. After the tenth post-operative year the death rate in patients who had carcinoma of the breast ran almost parallel with that of the general population.

AN OUTLINE OF TREATMENT

In discussing treatment in detail, I shall do it under rather unorthodox headings. Nevertheless, I do so in order really to be orthodox and not to be misunderstood.

1. *The Very Hopeful Case*

This commonly is the early, but not necessarily the very earliest case. In this patient the axillary nodes are still free from metastases, and the tumour is small and mobile, and is preferably placed in the lateral half of the breast. The fact that it has been there for several years is of less importance than the fact that the axilla is not yet involved. During the first few months a short history is actually indicative of a worse prognosis than a somewhat longer history. The explanation of this paradox lies in the fact that the patient seeks advice earlier, because the symptoms in her case are more pronounced; and the symptoms are more pronounced because the tumour is of a more active nature, a fact which is likely to become apparent on histological examination after the operation or at biopsy.

There is no proof that the youth of the patient influences the prognosis. Factors which do influence the prognosis are the anatomical situation, pregnancy and lactation, and a histologically active type of cell.

Radical mastectomy is the treatment of choice during this stage and for this type of case. But I must emphasize that the mastectomy must be a truly *radical* one. I am adamant about the principle that the earlier the malignancy, the more radical the excision must be, for it is in this type of case that we can expect a complete cure. It is here, much more than in the advanced case, that half measures may lead to failure in a patient who almost certainly could have been cured if we had not allowed ourselves to be influenced by the apparent infancy of the growth, and so adopted a less radical method. In my experience a local mastectomy is an incomplete operation.

Once histological examination has confirmed that the lymph nodes are free from disease radiotherapy need not be considered. Its application now is not only unnecessary, it may be detrimental. Irradiation is reserved for a much later period when, in a small percentage of cases, metastases may appear in the skin or elsewhere. The internal mammary nodes, however, may be irradiated in early cases if the carcinoma is located close to the sternum.

Ovariectomy should not be done now. I do not criticize those who use it at this stage, because on theoretical grounds it may well be that ovariectomy in the menstruating female will so change the immunity response to dispersed cancer cells that their activity is significantly subdued. But there is as yet no proof that the development of secondaries will be prevented.⁴

The baneful psychological and physical effects of ovariectomy should be avoided; its beneficial effects must be reserved for such of these cases as may eventually develop secondary lesions.

2. *Where a Mobile Tumour and Enlarged, but Mobile, Axillary Nodes are Present*

The prognosis has now deteriorated, but life expectancy is still 61.3% in 5 years' time, 42.7% in 10 years' and 31.1% in 15 years'. It is therefore obvious that we must still aim at complete eradication of the disease. With few exceptions it is universally agreed that this can be best achieved by a combination of surgical and radiological treatment. But there is some difference of opinion whether the operation should now be reduced to a *local* mastectomy, supported by irradiation of the axillary and other nodes, or whether it should still be a *radical* one supported by radiological treatment. There is also a difference of opinion whether radiological treatment should precede the operation or follow it. I firmly believe that the operation at this stage must still be a radical one. I do so because I have yet to see an axillary recurrence following extirpation of mobile enlarged nodes whether radiological treatment was given or not. I have, however, frequently seen supraclavicular nodes enlarge in these very cases after irradiation of both the axilla and the supraclavicular fossa. It happens in patients who had no palpable nodes above the clavicle before the irradiation. In my experience it is wrong at present to reduce the scope of the operation in favour of radiological treatment.

An eminent radiotherapist, McWhirter,⁵ has obtained impressive results by irradiation of the lymph nodes followed by local mastectomy. His results, however, do not equal—insofar as results are comparable—those obtained by the generally accepted methods of treatment.

As far as radiological treatment at this stage is concerned, I believe that it is best confined to the supraclavicular fossa, and the internal mammary area. I do not think it is necessary to irradiate the axilla in cases where the glands were mobile at the time of operation.

I further believe that the chest wall should not be irradiated at all in this type of patient. I must, however, emphasize that my remarks can only apply where the surgeon has done his job thoroughly. If the skin round the tumour is widely excised (disregarding whether a skin graft becomes necessary and the skin flaps are left with a minimum of subcutaneous fat) there need be little fear of local recurrences. A thick pad of subcutaneous tissue, which the radiotherapist prefers, should not be left. If it is, the number of local recurrences will increase. A recurrence in a skin underlain with scar tissue is not a matter of grave concern anyhow. It can be excised. Multiple recurrences can be irradiated. The results are much better where the skin has not been previously irradiated.

It is possible that an even more radical operation may become common practice in the foreseeable future if the results of those who are now practising this method can be proved to be superior to those of the less radical surgeon. In this ultra-radical operation the supraclavicular and the internal mammary nodes are also excised. The argument in favour of this extended operation is a sound one, viz. that in a considerable percentage of the cases where axillary nodes are involved, the internal mammary and the supraclavicular nodes are also involved. Against the extended operation there are two arguments. Firstly it is said that equally good results can be obtained by deep therapy to these two groups of lymph nodes. Secondly it is known that the operative risks are greater when the scope of the operation is thus extended. Although for the present I favour the ordinary radical or

Halsted type of operation, I sincerely welcome the fact that others are performing the ultra-radical one. In time we shall be guided by their results.

Ovariectomy and other forms of hormonal treatment have no place in this stage of the disease.

3. *The Locally Advanced Carcinoma*

I refer to the large, sometimes ulcerated, tumour with fixation to skin and/or deep fascia, and usually with enlarged fixed axillary nodes. This is a radiological problem and the advantages of ionizing radiation must be exploited to their maximum capacity in these cases. In the relatively small percentage of such cases where a previously non-operable tumour retrogresses to operable proportions, I believe one should operate, but not within 3 months after cessation of the radiological treatment. By then full fibrosis will have occurred, and one is not likely to do any harm. Although the standard operation now consists of a local mastectomy, I must admit that not infrequently I enter the axilla. But I do so only after thorough evaluation of the condition as seen on the operating table.

4. *The Widely Disseminated Carcinoma*

At this stage there is no more possibility of a cure being effected and our aim is palliation. The disease may be locally advanced. There may be ulceration, gross oedema, enlarged and fixed nodes in the axilla and the supraclavicular fossa. There may be enlarged lymph nodes in the opposite axilla and secondaries in bone in the chest, abdomen and cranium.

Operation plays no part except perhaps insofar as procedures to relieve pain may be adopted. Irradiation, however, can play an important part by controlling local spread and pain. The radiotherapist refrains from giving maximum doses in these cases. In fact he gives the minimum that will control ulceration, spread and pain. His aim is rather to reserve his treatment and to repeat it as often as is necessary, and wherever a local lesion gets out of hand.

HORMONE THERAPY

Hormone therapy has come to our aid as a powerful weapon in the advanced stages of the disease. Certain breast carcinomas are hormone-dependent, but as yet we have no means of determining whether a particular tumour is so dependent, other than by trial and error. When the tumour is hormone-dependent, the effect of hormone therapy is often profound, and much suffering can be relieved and life considerably prolonged.

Should this powerful weapon not be used at the earliest opportunity? I can only state that I have found no evidence that early hormonal treatment has any influence on the progress of the disease and the prolongation of life. I am aware that some surgeons are employing the hormones much earlier, but until we have the advantage of their results we must follow a course which has by now been reasonably

well tested. I must also sound a note of warning and point out that these new agents are potent and potentially dangerous. I have on several occasions been shocked by the speed with which a patient receiving this treatment has been rushed to a fatal end.

A Brief Statement on Hormonal Therapy

The Premenopausal Patient. As soon as it is obvious that the disease can no longer be controlled by irradiation, the first step is to perform double ovariectomy. Within 6-8 weeks we should know whether the effect is going to be satisfactory. If the operation produces no effect, it is unlikely that any further hormonal therapy—medicinal or operative—will be of use. If, on the other hand, the result should have been satisfactory and the disease should again show signs of advance, the next step ought to be hypophysectomy. If, after an interval of retrogression, there is a renewal of advance, androgens should be given. They are best given in the form of testosterone propionate, 150 mg. intramuscularly, twice a week for 10 weeks. Care must be exercised if the blood calcium is raised, if there is renal failure, or if ascites or hydrothorax is present. Unfortunately hypophysectomy is not such a practicable procedure. We, therefore, adopt a course which gives only slightly poorer results, but carries a lower mortality rate. After a successful ovariectomy we wait until deterioration reappears, and then go ahead with androgens. Finally when androgens cannot control the disease any more, an adrenalectomy is performed.

Patients 8 years and more Postmenopausal. Here we depend on oestrogens. Diethylstilboestrol, 5 mg. twice daily by mouth, is a satisfactory dose. Larger doses are no more effective, and will merely produce uterine haemorrhage. If oestrogens do not control the disease any longer, hypophysectomy is indicated; but in practice we commonly resort to double ovariectomy plus double adrenalectomy instead.

In spite of the almost miraculous results we obtain now and then, I very much doubt whether adrenalectomy is a procedure which has come to stay. It would be a different matter if we could determine beforehand which patients stood a chance to benefit by the operation. At present—apart from the occasional miracle that may take place—we are subjecting three women to all the pain of surgery and the removal from their family on the eve of their demise with nothing better in view than that one of them may live some 18 months longer. I am limiting the operation to patients with secondaries in skin, pleura and bones, and do not recommend it where metastases are located in the brain, the lungs and the liver. In any case, the decision to do the operation must not be postponed to a time when no more benefit can possibly be expected from it.

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