THE CASE FOR RATIONAL SURGERY IN CANCER

By F. M. LEHMANN, M.D.

Billroth once hoped that by eradicating every cancer cell at the onset he could cure malignant disease. Several generations of surgeons following in his steps have tried their best to attain this admirable aim, but in vain. We realize now that it cannot be done. The large-scale experiment in radical surgery has failed and the theory on which it was based has been found to be wrong. The theory of inoculation formulated by Halsted (1894) warns the surgeon never to cut through cancerous tissue when operating, to avoid the spread of cancer cells and to give the disease a wide berth. We know this fear is exaggerated. The body can take care of most circulating cancer cells (Schmidt, 1903). Cancer embolism is not cancer metastasis (Willis, 1952). Surgeons begin to realize that the good results after some radical operations are due to tissue resistance to cancer growth and not to removal of every bit of cancer (Gatch and Culbertson, 1952).

We are in need of a new theory as a guide to new experiments in cancer treatment, and we have not far to seek for such a theory. Our pathological knowledge has greatly advanced in the last 50 years. We have acquired a better understanding of the cancer cell and the cancer process as a whole. We know that cancer cells as such have no morphological or physiological characteristics which cannot be found in normal cells during regeneration (Ribbert, 1911; Fischer, 1937; Menetrier, 1926; Cowdry, 1940). Neither the property of indefinite growth (*vide* tissue cultures), nor of invasive, destructive growth (*vide* chorion-epithelium or osteoclasts) is uncommon with normal cells. Cancer cells are undifferentiated or maldifferentiated normal cells of the body and are—that is the proof—as such accepted by the body as long as they behave and do not become necrotic. Sooner or later when they begin to degenerate they are rejected by the body and treated as foreign bodies. A resorptive reaction sets in.

A malignant tumour thus carries its doom in itself. Being only a caricature of a tissue or an organ and performing only a farce of a function, the elements of the tumour are bound to de-

generate as soon as they start to function in response to functional stimuli; they are not competent like normally developed cells to react to the 'hormonal' stimuli carried to them by the ample blood supply of their stroma. While growth on the edges progresses, the central, more differentiated parts, begin to degenerate and elicitate a resorptive reaction.

All products of cell degeneration and necrosis lying in the tissues cause a resorptive inflammation and regeneration. This is a general biological law. By increasing the amount of cell detritus we can increase the intensity of inflammation or accelerate the rate of regeneration. This rule has many applications in general surgery and is also the basis of some treatments in cancer.

The rationale of cancer treatment can be formulated as follows: Bring on degeneration of cells (normal or malignant) in a tumour and its resorption will start. Continue stimulation after suitable intervals—to allow the reaction to take its course—and regression will become complete. There is nothing miraculous or specific about it. A malignant tumour regresses when and as long as products of tissue degeneration are present to keep the resorptive inflammation going provided the reacting tissues are left undisturbed and are not destroyed by irrational methods of treatment.

In other words, methods of cancer treatment work by stimulation of a natural healing process. We cannot force a cure by the choice of our destructive weapons, we can only—humbly and tactfully—follow the course prescribed by Nature. Nowhere in the field of medical practice can we find a stronger case for the venerable maxim of palliative treatment, *Natura sanat, medicus curat*, than in the field of cancer treatment. The following four examples may serve as an illustration.

Reaction to Radiation

Clinical experience in radiotherapy has taught that regression of malignant tumours after irradiation only takes place when a 'satisfactory' reaction is produced. The nature of this reaction has been known since the early days of radio-

therapy owing to the work of Rubens-Duval (1914) and has recently again been demonstrated in a very convincing manner by Jolles and Koller (1952). It is a connective tissue reaction. The experimental work of Murphy (1926), Cramer (1934) and others has established the fact that tumour regression under irradiation is not due to the direct lethal action of rays on every tumour cell—'while leaving the healthy tissues undamaged'—it can be brought about by the destruction of a few normal cells. Their degeneration leads to a resorptive reaction in the stroma and the surrounding tissues. Those who are not convinced may be reminded of the stimulation and cure of inflammatory lesions, both acute and chronic, by small doses of radiation (Desjardin, 1935). No cancer cells are present in these lesions, but the healing effect, clinically and histologically, is the same.

Reaction to Hormones

Cell degeneration through function is a physiological process, and cell function is regulated through hormones. Normally differentiated cells are competent to react to the hormonal functional stimulus in a proper manner and for a considerable time, maldifferentiated tumour cells are not. If, therefore, oestrogen in excessive doses is given in a case of breast cancer, the maldifferentiated and disorderly arranged duct cells of the tumour will start to function excessively and degenerate. At the same time, the normal, competent cells of the healthy breast will be able to cope with the excessive stimulus in a very different manner; they will show enormous stimulation with new formation of ducts and lobules. Husby and Thomas (1954), who made these interesting comparative studies, thought it 'almost paradoxical' that such an extensive proliferation of the normal breast epithelium should proceed at the same time that the neoplastic epithelium of the breast cancer in the same individual is dramatically decreasing in amount, for in many of the patients in their series who showed the greatest proliferation of the normal breast epithelium large deposits of breast cancer disappeared completely. This observation will appear less paradoxical if we imagine that the tumour tissue is trying to do exactly the same as the normal tissue but cannot and dies in the attempt. The necrobiotic cells are dealt with by the connective tissue cells and finally resorbed by the lymphatic tissues in the usual manner provided for by the organization of the body. As Emerson *et al.* (1953) concluded from their histological studies: Regression of tumours in the hormone treated patients is 'almost certainly the result of an unusual stimulation of a naturally occurring process of repair.'

Reaction to Cauterization

The stimulating action of cautery has long been observed and described. Halsted (1907) felt on safe ground when he wrote: 'I am indubitably convinced that the local and regional recurrences after incomplete operation which come as a rule with amazing rapidity when the knife has been used are, to say the least, relatively late in making their appearance when chemical or actual cauterization has been employed. I have several times had occasion to operate upon cancers which had been vigorously and repeatedly treated with caustics and to note the comparatively admirable condition, the freedom from cancer permeation of the surrounding tissues and of the axilla, whereas after incomplete operations with the knife the local manifestations of recurrence were almost invariably deplorable.' He mentioned with satisfaction that William and Charles Mayo endorsed his view that there was relative immunity from local metastasis with the employment of the cautery.

The observations of these witnesses were confirmed by other surgeons whenever they tried the experiment. Unfortunately very few did after 1907 owing to the role which radiotherapy began to play and the exaggerated hopes it aroused. When Byrne (1889) read his paper on 'Twenty Years Experience in the Treatment of Cancer of the Uterus by Galvanocautery,' telling how impressed he was by the systemic effects of this method—'even in hopeless cases cachexia and anaemia often temporarily disappear and despair gives place to buoyant hope'—the young Cushing, in the discussion, raised the pertinent question: 'Why should partial removal of an organ, the seat of malignant disease, result in cure in a greater proportion of cases than removal of the entire organ?' The only explanation that was tenable, he thought, was, that the application of some powerful caustic striking deeply into the surrounding tissue had some peculiar effect on the healing process.

How right he was. The great Czerny (1899) was of much the same opinion. He had observed better healing results since he removed cancer of the tongue by the thermocauter or treated afterwards the sanguinarily operated wound by the thermocauter. He had no doubt that the remarkable regression in these cases was related to the property of spontaneous healing.

Thirty years later, when the disastrous effects of intensive radiation became widely known, electrocautery was revived. The papers of Heitz-Boyer (1932), Kulenkampff (1933), Henschen (1934), Gernez (1935), Moersch and Bowing (1935) and Chlcnoky (1936) make fascinating reading. Strauss *et al.* (1935) fully confirmed the observations of Byrne. 'After the first or second application of

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diathermy the patient gains weight and the haemoglobin content and the red cell count of the blood are increased to normal levels. Even a patient who has lost a great deal of weight or is cachectic loses all the appearances that are characteristic of a person with advanced carcinoma.'

They also made the following important statement: 'Early in this work we coagulated too deeply and too thoroughly. We have come to the conclusion of late that it is best to coagulate superficially and not too severely, wait two or three weeks to see how much has been destroyed and then give a second, third or fourth application.' I think this is a method and a technique which every surgeon could safely use for his first experiments in rational surgery. It requires patience and devotion. The patient has to be kept much longer under observation and treatment as is the rule when radical surgery is performed. What has to be avoided in cancer treatment is hurry. One must not try to do too much in one session and not repeat the session too early. Above all, one must not 'combine' (stimulating) thermocautery with (radical) radiotherapy. Heitz-Boyer (1932) insisted that apprenticeship is required in the proper use of the electric knife. Epitheliomata are perhaps the most suitable object to get ac-

quainted with the reaction following slight tissue destruction.

Reaction to Toxins

That the toxins liberated by bacteria cause tissue degeneration followed by inflammatory reaction, nobody will deny. Nor can we dismiss the recorded observation of the older surgeons that during certain infections malignant tumours can regress and heal 'spontaneously.' Erysipelas was undoubtedly a frequent event after operations in the old days, and when a patient went through such an attack his tumour sometimes showed remarkable regression. Nowadays we see no erysipelas in our wards and if it occurred it would have no chance to act on the tumour because its natural, prolonged course would immediately be aborted by antibiotics. Coli infection has also been recognized as beneficial in cancer. Grey Turner (1943) found it significant that those cases of carcinoma of the colon which were complicated by abscess formation often did extremely well.

It seems that the extensive, and mostly 'prophylactic,' use of antibiotics in cancer surgery must be depreciated; it is not rational and should be reserved for extreme emergencies. When dealing with cancer, infections should not be repressed but

tolerated if not even invited. It was a shrewd idea of the surgeon Coley to try to imitate the action of infections by injecting toxins near the site of a malignant tumour. He and his followers were handicapped in their work by the prejudices of their time, most of the patients in their trials were unsuitable for this kind of therapy owing to the mutilating orthodox treatment they had received before. Their experiments had no sound theoretical foundation. It was more by chance and instinct that the technique employed led in some cases to surprising results (Coley-Nauts *et al.*, 1953). Another simple method of bringing about cell death and resorptive reaction is by strangulation of the blood supply. Allen (1940) has shown that temporary ligation of a tumour leads to its complete regression. Secondary infection may have been a supporting factor in these cases.

So much for the theory of stimulation which explains a variety of facts inexplicable by the theory of inoculation. The three principles of conservative and stimulative surgery which follow from the theory of stimulation are, of course, incompatible with the principles of radical and mutilating surgery which follow from the theory of inoculation, but they are rational and human. They are:

1. Surgical reduction of the growth to save the body the work of resorption.

2. Preservation of all tissues involved in the process of repair and resorption.

3. Stimulation of reactive processes during and after operation.

1. Local excision, not necessarily in one session, is the ideal to be aimed at; local recurrence an event to be expected but not feared. Recurrences can often be dealt with when they appear. Cancer is a chronic disease and more likely to be cured in frequent small steps than by a single surgical feat. Pack's philosophy of treating cancer wherever it is found is an excellent principle. So is Wangenstein's policy of second and third looks. Both would be much more useful if they implied under-radical rather than over-radical procedures.

We have yet to find out how often a growth actually recurs after repeated incomplete removal. Rotter (1889) had a patient who developed a massive local recurrence a few months after radical operation of her rectal carcinoma. She was in a desolate condition and all he could do was a curettage. She was sent home to die but returned, to his surprise, with another recurrence. This he curetted again and the lesion healed completely, as shown by autopsy two years later.

2. Preservation of lymphatics and of skin are the most important stipulation under this heading. It may be true that the disease spreads via the

lymphatics—if it does we cannot stop it—but it is equally true that its progress is stopped in the lymphatics and only in the lymphatics. More often than not the regional lymph glands, though palpably 'involved,' contain no cancer cells but show reactive proliferation due to resorption of necrotic tumour material. In the lymphatics, of course, the second and most important phase of the process of tumour resorption takes place, the disposal of the locally produced cell detritus.

If, by accident, a group of tumour cells breaks away and lodges in a lymph gland, it may develop into a metastasis, but this is growing in a highly reactive milieu of professional scavenger cells. Their action is strong enough to keep the growth confined, sometimes for years, if we let them. Gordon-Taylor (1948) recalls several patients with breast cancer and an axilla packed with 'infected' glands who have remained well for periods of 15 to 20 years in the absence of post-operative X-ray therapy.

The more we study the mysterious function of the lymphatics (Burnet and Fenner, 1949) the more we must realize that no tissue can live without lymph circulation. Patients can only survive after radical operations if they are able—one must wonder how—to regenerate the crudely dissected lymphatics. We certainly make it difficult, and often impossible, for the organism to secure its vital lymphatic circulation if we remove or destroy wide areas of skin and the fat tissue surrounding the lymph glands, the natural source of lymph vessel regeneration (Ritter, 1905; Hoepke, 1954).

On the other hand the lymphatics cannot be left alone in their struggle, they need help. Much is done already by excision of the primary tumour and 'calfatage' of its lymphatics by electrocautery (Champy and Heitz-Boyer, 1931). No fresh resorption work is coming in, the lymphatics can deal with the work in hand. A slight stimulus, repeated from time to time, is likely to give them further relief. We know that regional lymph glands in breast cancer regress under oestrogen treatment. This action is probably indirect through increased resorption of necrotic tumour material. By way of new experiments with this aim in mind we should be able to find the most effective and elegant method of stimulating lymphatic reaction.

3. Stimulation during operation is guaranteed by the use of the electric knife in cancer surgery. Some surgeons have adopted it already for their radical approach; they may find it even more suitable for the conservative approach in 'inoperable' cases. How to maintain stimulation for a long time after operation to promote regression in the draining lymphatics and beyond is a new problem recommended to the resourceful and enthusiastic

surgeon investigator. Grey Turner, in a letter written shortly before his death, thought of using Coley's mixed vaccine for this purpose—not a bad idea. Another, more specific method occurred to me would be the use of the corresponding normal organ in the form of a pulp or extract injected weekly or two weekly near the tumour site.

Summary

The experiment of radical cancer treatment based on the theory of inoculation has failed. The case for palliative cancer treatment is based on the theory of stimulation. This theory explains:

1. The success and failure of radiotherapy.
2. The action of oestrogen in breast cancer.
3. The superiority of incomplete removal by electrocautery to complete sanguinary removal of malignant tumours.
4. The effect of bacterial toxins on cancer.
5. It encourages further research in cancer surgery.
6. It enables the surgeon to give relief in every case of cancer.

If the distinction between 'operable' and 'inoperable' stages falls every case of cancer becomes amenable to palliative and stimulative treatment.

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