RADIUM TREATMENT IN CANCER.

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The treatment of cancer by means of radium is still in the experimental stage. During the past few years valuable work has been done by physicists regarding the physical properties of radium and much of this information has proved to be of definite value to therapeutists. The attention of the latter has been directed to various questions concerning technique and dosage with the result that radium therapy is being established on a sure basis. On the experimental side important work has been done regarding the action of radium on normal and cancerous tissues.

During this time the popularity of radium in the treatment of cancer has waxed and waned. At first it was hailed as a certain cure when the first early results came out producing an unwarranted degree of enthusiasm. Certain disappointments were encountered, and the limitations of the new treatment were realized and the sceptics were very critical. However, radium is beginning to find its true level and is establishing itself as an important branch of therapeutics. Time is essential to prove its limitations and to determine the rules which govern its application.

The National Radium Commission is doing important work in carrying out an investigation on a national scale into the value of radium therapy in cancer and the best method or methods of rendering this treatment. With this object in view the Commission has distributed amounts of radium to Centres throughout the country which have been established in university towns or places where special facilities are available to ensure that the radium is used to the best advantage. The majority of the London hospitals have quantities of radium, and the Mount Vernon Hospital and the Radium Institute form a Post-Graduate school for the country. This investigation instituted by the Commission will, it is hoped, yield results concerning the radium treatment of cancer which will prove of the greatest value to the profession. The conclusion has been reached that at least five years must elapse before a reasonable estimate can be placed on the results. Recently, a Preliminary Report on Radium Treatment in Cancer of Certain Sites⁽¹⁾ has been published by the Commission; references will be made to the work in this paper.

The object of this paper is to show what is being done with radium in cancer of the more important sites in the body. In order to appraise this correctly reference is made to the results obtained with excisional surgery. Throughout the country many are working on problems connected with the causation and treatment of cancer. Clinicians and laboratory workers are engaged in close co-operation and much important data is accumulating. Professor G. E. Gask⁽²⁾ has called attention to the need for an organized campaign on a national scale against cancer and the necessity for close co-operation in some form between the various bodies engaged in the fight. If further advance is to be made along the cancer front it is essential that our present methods of treatment are evaluated, hence it is important that cancer statistics should be compiled on a national scale. This work is being done for radium therapy and a similar investigation should be carried out for excisional surgery.

Carcinoma of the Breast.

Reference to the Registrar-General's Statistical Review of England and Wales for the year 1933 shows in that year 32,735 women died from cancer of various organs and of this number 6,551 died from cancer of the breast. These figures convey an impression of the importance of this disease.

The value of excisional surgery. It is very unlikely that the results from excisional surgery alone will be improved upon in the future and it is pertinent to enquire as to the order of these results. If the results of cancer of the breast are assessed it is essential to classify the patients into stages according to the anatomical extent of the growth. A useful classification is the following:—

Stage 1.—The carcinoma is limited to the breast and does not involve the skin or underlying structures.

Stage 2.—The carcinoma has invaded the axillary lymph glands.

Stage 3.—The carcinoma is more widespread. There is attachment to the pectoralis major muscle or there is ulceration of the skin overlying the breast. Lymph nodes in other situations than the axilla may be involved.

Various operations have been designed for the treatment of this disease and they may be grouped in three categories as follow:—

(1) Local excision of the breast. (2) Excision of the breast together with the axillary lymphatics. (3) Excision of the breast together with the underlying pectoralis major and minor muscles and the axillary lymphatics. The last complete operation is most commonly used. In Table 1 the results obtained by operations 2 and 3 in each stage of the disease are set out.⁽³⁾

Table 1.—Cancer of Breast.

The 3 year net survival rates* in each stage of disease for each method of treatment.

Type of operation.	3 year net survival rate in percentages.	
	Stage 1.	Stage 2.
1. Excision of breast and axillary lymphatics	50.0	41.4
2. Excision of breast, pectoral muscles and axillary lymphatics	65.4	34.5

If the mass of patients applying for treatment at a large hospital is considered it is found that the 3-year crude survival rate† is 46 per cent. for patients in all stages treated by all methods of excisional surgery.⁽⁴⁾

* The term net survival rate is the proportion of patients alive, irrespective of the presence of disease, to the total number of patients treated after deducting the number of patients dead from causes other than cancer and patients lost sight of.

† The term crude survival rate makes no allowance for patients who are dead from causes other than cancer and patients lost sight of.

These are the results obtained with excisional surgery in cases observed for 3 years. It is admitted that this period of time is too short to provide a stable end-result; nevertheless, it does indicate the way the final result will turn out. It will readily be agreed that the results are not good enough and it is difficult to see in what way they can be improved by further modifications of surgical technique. It appears therefore that we must base our hopes for the future on other methods of treatment or a combination of methods.

The value of radium. It has been proved that complete regression of the primary growth in the breast can be attained with radium therapy. Keynes⁽⁹⁾ has elaborated a technique in which interstitial irradiation is employed. The primary tumour is completely irradiated and the lymphatic areas are successively dealt with. Thus the axillary lymphatics are extensively irradiated in such a way as is hoped to include the apical, subpectoral and subscapular lymph glands, together with the lymphatic vessels which converge on the axilla from the primary tumour. The supra and infra-clavicular and the anterior mediastinal lymph glands are also irradiated. This technique has been extensively used throughout the country.

In 1933 Ward and Durden Smith⁽⁶⁾ wrote that the radium treatment of early operable cases—that is, cases in stages 1 and 2—was still under trial. In this connection the results recently published by the National Radium Commission are of the greatest interest. The results have been evaluated in 557 patients with cancer of the breast as a 3-year net survival rate. These patients have been graded according to the anatomical extent of the disease as already defined. The results obtained in each stage of the disease with all methods of radium treatment are shown in Table 2.

Table 2.—Cancer of Breast.

The 3 year net survival rate in each stage of the disease with all methods of radium treatment.

Stage of disease							3 year net survival rate in percentages.
I	...	...	...	...	...	...	64.0
II	...	...	...	...	...	...	39.9
III	...	...	...	...	...	...	24.9

The present position based on the 3-year net survival rate in cancer of the breast is as follows. It appears from the figures to which attention has been drawn that the same result will be given in stage 1 of cancer of the breast by radium and the operation of excision of the breast, pectoral muscles and axillary lymph glands. Involvement or otherwise of the axillary lymph glands is the touchstone on which the prognosis must be assessed. There is no doubt that if the disease is strictly local it can be eradicated with good results, but if it has spread to the axillary lymph glands the prognosis assumes an unfavourable complexion. From the figures quoted it would appear that interstitial irradiation of the breast gives a little better result than does excisional surgery. In the advanced stage 3 of the disease radium therapy is of definite value whereas excisional surgery holds out no permanent relief to the patient and at best is only a palliative measure. The 3-year net survival rate in these patients treated by radium is 24.9 per cent. Many of us have witnessed the improvement in large ulcerating tumours of the breast

after radium therapy and how masses of lymph glands in an inoperable condition can be controlled in many cases.

The combined treatment by radium and excisional surgery. It is possible that in the future, work will be increasingly done with combined radium and excisional surgery. Sampson Handley⁽⁷⁾ buries radium tubes along the line of the internal mammary lymph glands at the time of operation. The results published in the Report of the Radium Commission show that better results are obtained in the advanced stage 3 of the disease when radium therapy was combined with excisional surgery. It is known that in certain cases obviously inoperable growths in the first instance respond well to radium therapy and render excision possible. There is scope for further work in this connection.

The necessity for early diagnosis. If the results of treatment of cancer by radium or excisional surgery are to be materially increased it is essential that more patients be seen when the disease is still localized to the breast. It is believed by many that in the early stages, cancer is a local disease and becomes disseminated with the passage of time. In the Report of the Radium Commission the duration of symptoms between the onset of disease and application for treatment has been determined in 557 patients. It is a lamentable fact that only 21.6 per cent. of these patients applied for treatment less than three months after the lump had been discovered and it is shown that the survival rate is more than doubled in those patients who apply for treatment less than three months after detecting the lump, when compared with the survival rate in those patients who delay for six to eight months.

F. M. Smith⁽⁸⁾ in a recent investigation found that in cases of breast cancer there was an average delay of 10 months between the onset of symptoms and the time the patient was admitted for operation. There was an average delay of 3.2 months between the onset of symptoms and the time the patient first consulted her own doctor. The time lost between the first consultation with her doctor and the time she was admitted to hospital for operation was on the average 8.6 months. We must learn to recognize cancer of the breast in the very early stages and institute the appropriate treatment without delay.

Cancer of the Tongue.

It is to be deplored that the results achieved by excisional surgery in cancer of the tongue are so uniformly bad. A survey of the published results of treatment from the time of Butlin onwards shows that the surgery of cancer of the tongue has made but little progress. The counsel of Butlin is worth consideration. In 1909 he wrote "the results of operations for the removal of recurrent disease, whether of the tongue or glands, have been so bad that operators are counselled to make the first operation as complete as possible in the belief that the only hope of the patient lies in the thorough manner in which the operation is performed."

Professor Gask has compared Butlin's figures with those of St. Bartholomew's Hospital. Butlin treated 197 cases and 27.9 per cent. were alive at the end of 3 years; this is compared with the recent figure of 35.7 per cent. at St. Bartholomew's Hospital.

The results of radium therapy. Bearing in mind the results obtained with excisional surgery, it is of interest to consider the value of radium therapy in this disease. In the Report of the Radium Commission the results from radium therapy are set out in 322 cases of cancer of the tongue. A system of classification has been worked out according to the stage of the disease, and the results in each stage have been determined.

The importance of early diagnosis is shown by the relatively high 3-year net survival rate of 40.0 per cent. which has been obtained in stage I cases in which the growth was limited to the tongue. If the disease has spread to adjacent structures such as the floor of the mouth the survival rate is much diminished at 21.4 per cent. The importance of involvement of the regional lymph glands is shown by the low survival rate of 12.9 per cent. obtained in this stage of the disease. This was recognized by Butlin in 1909 when he wrote, "The future of the operative surgery of carcinoma of the tongue undoubtedly lies in early diagnosis of the disease and in the routine removal of glands before they are obviously enlarged." When the disease has progressed so as to involve the mandible only 2.9 per cent. survive 3 years.

Interstitial irradiation of the primary growth is the usual method of treatment of these cases and it is remarkable to see the way the carcinoma disappears, although this regression is not permanent in all cases. During the succeeding days after radium is inserted the tongue becomes covered with a yellowish membrane. There is often a certain degree of oedema and inflammation of the tongue which quickly subsides. The induration around the growth gradually disappears and healing of the ulcer commences from the periphery. In many cases after adequate treatment the tongue is almost normal in from 4 to 6 weeks.

The difficulty in these cases lies in the adequate treatment of the regional lymph glands. It has been suggested that treatment should vary according to whether the cervical lymph glands are palpable or not. I believe this to be fallacious for it is an unfortunate fact that secondary deposits of carcinoma may be present in lymph glands without causing clinical enlargement. In a series of cases studied at St. Bartholomew's Hospital⁽⁹⁾ it was shown that of 34 lymph glands containing deposits of carcinoma microscopically there were 3 which were not palpable clinically. It was also shown that if lymph glands are palpable, the greater proportion contain carcinoma cells microscopically, the percentages being 56 with carcinoma against 43 without carcinoma.

At the present time various methods are employed for the treatment of the regional lymph nodes and in view of the facts presented treatment should be carried out on the neck in every case irrespective of the time the disease has been in evidence.

Irradiation of the neck. Interstitial irradiation by means of radium needles is sometimes used. The needles may be introduced by skin puncture but it is often difficult by this means to get a complete and evenly distributed irradiation. It is preferable to expose the glandular area in the neck by open operation and radium needles are buried in the tissues and the wound closed. Surface irradiation of the neck has been employed by means of a Columbia paste collar to which

radium needles are fixed. This collar can be worn by the patient with a certain degree of comfort.

Block dissection of the neck. Many surgeons prefer to excise the cervical lymph glands after treating the primary growth with radium. This method has the advantage in that the lymph glands can all be exposed and carefully dissected away. In certain cases deep X-ray therapy has been used in the treatment of the regional lymph glands either alone or in conjunction with excisional surgery. At present it is impossible to state which method of treating the lymph glands gives the best results. This is an urgent problem demanding solution and light may be cast on it by the results obtained from bomb therapy.

Cancer of the Cervix Uteri.

A great amount of attention has been given to the treatment of cancer of the cervix uteri with radium and a large amount of work has been expended. In the early days of radium therapy it was found that cancer of the cervix uteri was radio-sensitive. This fact, together with the easy accessibility of the growth, led many to use radium in this field and encouraging results were obtained. In the first place only, advanced growths were treated in this way, but later the more early cases were subjected to the treatment.

The first radical operation for carcinoma of the cervix uteri by the abdominal route was devised by Wertheim in 1898. The object of this procedure was to remove the entire uterus together with the cellular tissue of the pelvic floor and the lymph glands involved. At first the operative mortality from this operation was as high as 21.7 per cent.; in 1930, however, Bonney⁽¹⁰⁾ reported that in his hands it was 8.1 per cent. Bonney also determined the net survival rate in all cases for 5 years and found it to be 25.5 per cent.

The results of radium therapy in cancer of the cervix uteri. In order to evaluate the results of radium therapy in this disease it is essential to grade patients in stages according to the anatomical extent of the growth. The classification which has been universally adopted is that defined by the Radiological Sub-Commission of the League of Nations Health Organization:—

- Stage I. The carcinoma is strictly limited to the cervix uteri.
- Stage II. The carcinoma is spreading into one or more fornices.
- Stage III. There is nodular infiltration by carcinoma of the parametrium on one or both sides.
- Stage IV. There is massive carcinomatous infiltration of both parametria.

A detailed consideration of the technique employed in radium therapy in cancer of the cervix uteri is omitted. The method of treatment generally employed is the combined use of intra-uterine and vaginal applicators. The quantity of radium used and the time over which the dose is spread are variable. The treatment of the regional lymph glands has not yet been standardized; deep X-ray therapy and the intra-abdominal insertion of radium have been employed. In the Report of the

Radium Commission the results obtained with radium therapy in 590 patients are analysed. Their figures are set out in table 3.

Table 3.—Cancer of the Cervix Uteri.

The 3 year net survival rate in each stage of disease with all methods of radium therapy.

Stage of disease	Percentage net survival rate.
I	60.8
II	48.1
III	32.6
IV	11.8
All stages	39.4

The future of Radium Therapy.

It is quite impossible to forecast the eventual place which radium will hold in therapeutics. From the work which has already been carried out it appears that we have in radium a powerful weapon in the warfare against cancer. It is essential that we should know all about its properties and control its activities and put them to the best possible advantage. A great deal of good pioneer work has been carried out in the past few years. It is quite possible that many methods of rendering radium therapy which have been used in the past will become obsolete in the future. All the time the evolution of treatment is proceeding. The relative advantages of each method are being determined and the results assessed, but this will take considerable time.

Attention at the present time is being focussed on high voltage X-rays and radium bomb therapy. Mass radiation is now being given an extended and thorough trial, and if the results are adequate, the advantages of this technique are apparent. By this means a solution may be found to the problem concerning the best method of treating glandular metastases. It may be possible to treat cancer in deep seated organs such as the stomach and other abdominal viscera.

Physicists are occupied with the problem of high voltage X-rays, but it appears that a good deal of further work must be done before this can be safely applied to the treatment of patients.

Conclusions.

An attempt has been made to convey an impression of the present position of radium therapy in the treatment of cancer of the breast, tongue and cervix uteri. Attention has been drawn to recent work on the subject. A plea is made for earlier diagnosis in cases of cancer. A glimpse is given of certain possible developments which may eventuate in the years which lie ahead.

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