X-RAY THERAPY IN CARCINOMA OF THE LUNG*

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(With Special Plate)

Statistical evidence accumulated during the last ten years points to an increase in the incidence of primary carcinoma of the lung. It is now known that this condition constitutes 5 to 10 per cent. of all carcinomata, and for this reason is comparable with carcinoma of the large bowel and with other carcinomata which have received much more attention. An appreciation of this fact leads us to a consideration of the various possibilities in regard to treatment.

It is apparent that the choice of treatment lies between surgery and radiation therapy, and from a review of the somewhat extensive literature on the subject it would appear that most writers name surgery as the method of choice. In this respect, however, it is conceded by all that where the disease originates in a major bronchus surgical measures are possible only in the very early case. Apart from this, radical removal is possible only in the parenchymal type of lesion, and since this constitutes some 10 per cent. only of all cases the sphere of surgery would seem to be limited. Furthermore, radical surgery, even at the hands of the expert, carries with it a primary operative mortality which is quoted by various authors as 30 to 50 per cent. Graham,¹ in putting the case for surgery, reports only one case in the literature alive five years after lobectomy for pulmonary carcinoma. Carlson and Ballou² were able to find only thirty-five cases in which pulmonary carcinoma had been extirpated surgically, and out of these only six patients lived one year or longer. Young³ recently reported a patient alive three years after lobectomy for carcinoma.

On the other hand, Kernan⁴ reports a case of histologically proved bronchial carcinoma in which the patient was alive and well six years after high-voltage x-ray treatment, and in the series of forty-two cases recorded by Leddy and Vinson⁵ ten of the patients who received x-ray therapy only were alive from fifteen months to four years after the diagnosis was made. Holfelder,⁶ while not recording survival beyond three years, draws attention to the marked symptomatic relief which is obtained after radiation therapy, and this view is confirmed by Roberts,⁷ who, despite the fact that life may not be appreciably prolonged, considers that the relief secured in relation to pain and cough justifies x-ray treatment even in advanced cases.

A Glasgow Investigation

During the years 1934 and 1935 thirty-six cases of primary bronchial carcinoma were referred for treatment to the x-ray department of the Western Infirmary, Glasgow. In five of these the condition was so advanced that treatment was not undertaken; and all of these patients died within two months. In sixteen cases the condition was such that intensive treatment did not appear to be justified, and palliative measures only were adopted. These were designed to give the patient symptomatic relief without adding to his discomfort by the production of a severe skin reaction. The average survival period in this group was three and a half months.

In the remaining fifteen cases radical treatment was attempted. The first seven patients were subjected to a treatment to which one might apply the term "semi-

radical," in that it extended over a period of three weeks only, with an assessed tumour dose of 3,000 r. The average survival period in this group was five months. In the other eight patients a more radical procedure was adopted: the total period of treatment was extended and the total dose delivered to the tumour zone was correspondingly increased. In the later cases it was found possible to deliver an estimated dose of 6,000 r to the tumour zone in a period of six weeks. The response in this group has been appreciably better: four of the eight patients are still alive seven to twelve months after treatment, and the average survival period of the four patients who have died was extended to eleven months.

These observations would suggest that with improved methods an increased survival period is possible, and this suggestion has proved a stimulus to further endeavour. The following cases illustrate the type of response which has been obtained.

Case I

A female aged 59, when first seen in February, 1934, gave a history of cough and pain in the chest of four months' duration. For some weeks before she came under observation she had become progressively short of breath. There was no history of haemoptysis and no loss of weight. Clinical examination revealed complete dullness of the left side of the chest, which x-ray examination showed to be due to almost complete collapse of the left lung, apparently associated with a tumour in the region of the left hilum. Lipiodol revealed a definite bronchial stenosis in relation to the tumour mass. X-ray treatment was begun in February, 1934, through four ports of entry converging on the tumour mass. The response was satisfactory; cough and pain subsided, and within two months the lung was expanding, diaphragmatic excursion was practically normal, and there was a decrease in the size of the tumour mass. In July, however, the patient developed generalized metastases, to which she succumbed in October, eight months after treatment was started. During the subsequent course of the disease there was no recurrence of the pulmonary symptoms (see Plate, Figs. 1, 2, and 3).

Case II

An iron moulder aged 55 was admitted to hospital in October, 1934, complaining of pain in the chest of six weeks' duration, which took the form of a constant ache with acute exacerbations. There was an irritable cough, but no history of haemoptysis. Clinical examination did not reveal any signs in the chest and the blood picture was normal. X-ray examination, however, showed an apparently solid tumour in the middle zone of the left lung field towards the hilar region, but extending out a considerable way towards the lung periphery. There was no evidence of pleural effusion. Lipiodol examination carried out at this time indicated an obstructive lesion in relation to the bronchi supplying the lower portion of the left upper lobe. X-ray treatment was started in October, 1934, five ports of entry being employed. Within a few weeks the patient obtained symptomatic relief, and at the end of two months there was definite evidence of regression of the primary growth. The patient continued to improve; cough and pain disappeared, and he put on weight. His general condition remained satisfactory until the spring of this year, when he developed a metastasis of the spine, to which he succumbed in April—eighteen months after treatment was begun (see Figs. 4 and 5).

Case III

A police officer aged 44 was admitted to hospital in May, 1935, with a history of pain in the right shoulder, cough, and slight haemoptysis of three months' duration. Clinical examination revealed a zone of dullness corresponding with the right upper lobe, and x-ray examination showed complete obscuration of the upper half of the right lung field, apparently due to upper lobe collapse. X-ray treatment was instituted, and the patient improved steadily. The pulmonary lesion regressed and the lung re-expanded. The patient's cough disappeared and the haemoptysis cleared up entirely. He has gained weight, and is now back on full duty, symptom-free for over a year (see Figs. 6, 7, and 8).

* Read in opening a discussion in the Section of Radiology at the Annual Meeting of the British Medical Association, Oxford, 1936.

Case IV

A seaman aged 50 was first seen in August, 1935, when he gave a history of occasional pain in the chest during the previous three weeks, associated with slight haemoptysis. There had been no loss of weight, and the patient's general condition was good. X-ray examination at this time revealed a solid tumour in the left upper zone midway between the hilum and the periphery. X-ray treatment was started at once, five ports of entry being employed. The lesion responded well, and regressed almost completely. The pain in the chest disappeared, there was no further haemoptysis, and the patient returned to his work. He is alive ten months after treatment, and there has been no recurrence of his pulmonary symptoms.

Rationale of Treatment

In the evolution of radiotherapeutic technique for the treatment of malignant disease there has, of necessity, been considerable divergence of opinion regarding the most desirable method to employ. During the last five years or so, however, one has seen evidence of more general agreement among radiologists concerning what one might refer to as the fundamental principles. Of the individual factors involved probably the most important is total physical dosage. It is appreciated that from a purely biological point of view this must, of necessity, vary with the total duration of the treatment, but experience is gradually teaching us that for any given period of treatment there is, for different groups of tumours, a lethal dose which must be attained throughout the tumour zone before permanent regression of the lesion may be anticipated. The possibility of reaching this dosage level within any given period is dependent on a number of factors, and leads at once to a consideration of the second most important factor—time. It is almost universally held, particularly in relation to x-ray therapy, that a prolongation of the total period of treatment produces results of enhanced therapeutic value.

There is as yet insufficient evidence to determine whether these results are due to the fact that the longer period of treatment permits the delivery of a larger total physical dosage to the tumour zone without undue damage to the normal tissues, or whether the extended period, with the consequently greater number of individual treatments, increases the probability of all the malignant cells being irradiated during the vulnerable phase of their mitotic cycle. Furthermore, while accepting the principle of daily treatments with protraction of the total period, there is still much work to be done regarding the possible importance of extending the time of each daily administration, or, in other words, of treating at lower intensities.

There is now general acceptance of the view that any attempt at radical treatment must take the form of a single continuous course of irradiation. The dosage necessary is such that it has to be carried to the limit of tolerance of the normal tissues, and while these recover almost completely they are never able to stand again the same dosage, and it follows, therefore, that should the first attempt fail there can be no second one. A rigid observance of this principle is particularly necessary in any attempt at radical treatment of carcinoma of the lung. The lung tissue will probably just recover from the tumour lethal dose, but this tissue, if subjected to a subsequent course of treatment, will break down and a necrotic lung abscess will ensue.

In planning the scheme of treatment every effort should be made to secure homogeneous irradiation throughout a zone which is calculated to include all the malignant tissue. To assess this is a matter of the greatest difficulty, and yet on this decision, probably more than on any other, depends the success of the treatment. A scheme which fails to embrace the entire tumour zone is naturally

foredoomed to failure, but it is equally true that the indiscriminate irradiation of a large volume of tissue will lead to failure—first, because the local tolerance limits of normal tissue decrease appreciably when a large volume is irradiated, and it then becomes impossible to attain the tumour lethal dose; and, secondly, because the volume of tissue irradiated may be so large that the patient will succumb to the general effects of irradiation. It is apparent, therefore, that there is a physical limit to the size of a lesion for which treatment can be undertaken, and it would, in fact, appear to be a mistake to attempt radical measures where the lesion is obviously large.

In arriving at a decision in this respect cognizance must be taken of the fact that an apparently extensive opacity is not necessarily all due to tumour, and that it may be due to collapsed lung following stenosis of the bronchus. The presence of bronchial stenosis may be determined by lipiodol, and films taken at higher kilovoltage may be successful in outlining the tumour mass. On the other hand, it must be borne in mind that in the interval between the onset of symptoms and the patient seeking advice spread to the mediastinum has in all probability occurred, and, as a rule, therefore, the scheme should be such that the mediastinum will be included within the treated zone.

If we accept the principle of protracted irradiation and decide to treat for a period of six weeks or longer, then, from observations regarding the behaviour of carcinomata in other situations, it would appear that we must be prepared to carry the dosage in the tumour zone to a level in excess of 6,000 r. To do this without producing permanent skin damage it is necessary to use at least five ports of entry. Some radiologists would prefer to use a larger number, but this means that the areas must be smaller, and in my opinion this increases the risk of failure through inaccurate direction of the beam; apart from the fact that even with theoretically perfect alignment the use of small fields limits the zone, which is effectively irradiated at the depth.

In planning the scheme of irradiation therefore one must first consider the extent of the volume of tissue at the depth which must be irradiated. This will consist of a cylindrical or spherical volume, and, in conjunction with the focal skin distance, will determine the size of the rectangular or circular ports of entry on the skin. In general terms it will be found that at focal skin distances of 40 to 50 cm. a port of entry 8 by 10 cm. will be selected, since at that depth converging beams of this size will embrace a cylindrical volume of tissue 10 cm. in diameter by 12 cm. long. It is doubtful whether, with apparatus operating at the 200 kV level, it is possible to irradiate successfully a volume larger than this. This opinion may be subject to revision in relation to plants operating at higher potentials.

Attention has already been directed to the necessity of avoiding skin damage, and here I should like to stress one point which in the past has not received the consideration it deserves. In a number of clinics it is the custom to treat one, or at most, two areas per day, with the result that each individual area receives treatment every second, third, or even fourth day only. While inevitably entailing more work, there would appear to be little doubt that by irradiating all areas each day an appreciably greater degree of skin tolerance is obtained, and for obvious reasons this is a factor of considerable importance in the treatment of intrathoracic lesions, where considerable difficulty already exists in relation to the delivery of a tumour lethal dose within the limits of tolerance of the skin of the chest wall.

In conclusion, I should like briefly to refer to the selection of cases. I have suggested that patients may be divided into three groups. First, those in whom the

disease is so advanced that simpler and more effective palliation may be obtained by morphine. Secondly, those patients in whom there is loss of weight, which indicates probable metastases, or, while their general condition may appear reasonably good, the extent of the lesion as determined by its physical dimensions or the existence of pleural effusion is such as to preclude any hope of successful radical treatment. In this group, as has been pointed out by other writers, palliative irradiation is justified, and, in my opinion, this is achieved most readily by a short course of treatment, extending at most to five days. In this respect one must adhere to the rule that palliation must not be worse than the disease itself, and for this reason no severe skin reaction should be incurred. Dosage should, however, be carried right up to the level of a mild erythema, and it will be found that at this level quite effective palliation may be obtained. Lastly, there are the cases in which an attempt at radical treatment would appear to be justified. The patient must show no signs of debility arising from the disease; there must be no loss of weight; and the lesion must be of such limited extent that on assessment it will be possible to include it entirely within the irradiated zone.

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Clinical Memoranda

Detachment of the Retina

Retinal detachment without a visible hole is usually considered to have a bad operative prognosis for two reasons: first, there is no direct guide to the actual seat of damage; secondly, instead of being able to seal the hole directly, at most one can only hope that it will become secluded by the retina falling into contact with the area of operatively inflamed choroid. A case of recovery of full field and 6/6 vision may be worthy of record.

CASE REPORT

A girl, aged 17, came to the Free Eye Hospital, Southampton, in December, 1934, when her vision was found to be 6/6 in each eye separately, with a plano in the right eye and a lens of -0.5 dioptries combined with +0.75 dioptries cylinder, axis vertical in the left eye.

On April 11th, 1935, she returned, complaining that the sight of the left eye had become very much worse; testing her with her glasses it was found to be 6/36 (one letter). There was no recent history of accident, but four years before she had had a blow from a cricket ball on the left side of the head. Looking at my hand, held up at one metre, she could not see the palm or fingers while gazing at the wrist; and a perimeter chart showed loss of the field above the horizontal line. A flat detachment of the retina could be seen, forwards and below, but there was no appearance of a hole, nor was any found at any subsequent examination, in spite of careful search.

The patient was admitted under atropine, and kept quiet in bed for four weeks, at the end of which time, as the appearances were still the same, I did a diathermy surface cauterization at the 3.30 to 5.30 position on a clock-face, placing a curved "barrage" 6 mm. away from the limits of the ciliary body. The middle of the crescent-shaped area thus enclosed was then punctured with a red-hot electro-

cautery, and when the subretinal fluid had drained away the red cautery was again inserted for a moment to the depth of 2 mm., after which the wound was closed by a conjunctival flap.

The patient was kept in bed with a double bandage for eight days, when it was seen that the retina was reattached; the double bandage was retained for three more days, and then was replaced by pin-hole spectacles with side shields, which were made by using two of Dobson's squint occluders, the latter being eye-cups of thin black celluloid, which can be perforated in the centre with a hot knitting-needle, and slid along a cross-bar to suit the interpupillary distance.

She wore these at home for a month, and then vision with her spectacles had returned to 6/6, the field was full, but a small area of detachment could still be seen, far forward below.

In July, 1936, or nearly twelve months after the operation, I saw the patient again. The vision is perfectly restored, being 6/5 without spectacles; the field shows no loss of contour whatever. The retina, far forward, shows the marks of trauma from operation, and as this site cannot be demonstrated in the field it would seem that a complete cure has been attained.

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Coloured Lenses in Refraction

Many children disapprove of strangers and frequently express their disapproval in no unmeasured voice; especially is this so if they first make the surgeon's acquaintance in the dimness of a room prepared for retinoscopy. Much time must frequently be spent in overcoming their shyness and in diverting the child's attention from oneself. In private practice it is possible to spend most of the period of consultation in making friends with the small patient with a consequent accuracy and rapidity of examination when confidence has been gained. Nor is it necessary for the child to be brought into a darkened room. On the other hand, all those who have to do clinic work will realize that it is impossible to allow half an hour, or even a half of that time, for each child; that in most cases the child must be brought from the daylight into a darkened room, and, with pupils dilated from the previous use of atropine, the examination has to be commenced before dark adaptation has taken place.

Most children are responsive to colours, and to that end coloured toys in a consulting room "break the ice." In clinic work the nearest we can approach to the ideal of private practice is to endeavour to attract the attention of the child by the light reflected from the retinoscopy mirror. Some children look at it once and decide the performance is not going to be attractive enough to warrant their interest. In an endeavour to overcome this I used to shine the light through the red and the green glasses from the trial case held side by side, first through one colour and then the other. This was more attractive to the child, and it occurred to me that if they were lenses I should have some idea of the refractive error.

I have therefore had made a set of tinted lenses, and have found that nearly all children forget their surroundings in their interest in the colours. In experimenting over a wide range of coloured glass I had to obtain colours which were not too dark to obliterate the shadow but were yet dark enough for the child to perceive that a colour was present. Ultimately I selected the following colours in these strengths.

+ 2 D Sph.: Amber.	+ 4 D Sph.: Blue No. 4.
+ 2.5 D Sph.: Soft-lite No. 4.	+ 4.5 D Sph.: Nile green.
+ 3 D Sph.: Rose.	+ 5 D Sph.: Yellow.
+ 3.5 D Sph.: Pale green.	

The lenses are plano tints, to each of which is cemented a plano-convex lens of a different strength. This keeps the depth of colour the same throughout the lens. The lenses are graduated in half-dioptres, as in restless children

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FIG. 1.—Case I. Before treatment, showing complete collapse of left lung.

FIG. 2.—Case I. Bronchial stenosis outlined by lipiodol.

FIG. 3.—Case I. Three months later, showing almost complete re-expansion of left lung.

FIG. 4.—Case II. Outline of solid tumour before treatment.

FIG. 5.—Case II. Appearance eleven months later, showing fibrosis of lung in treated zone.

FIG. 6.—Case III. Condition before treatment.

FIG. 7.—Case III. Six weeks later.

FIG. 8.—Case III. Six months later.