The experience of X-ray workers goes to prove that, when used early, X-ray treatment holds out the promise of a certain degree of success. The logical outcome of such experience leads one to suggest the following definite rules for the guidance of all who wish to use X-rays as an adjunct to the routine treatment of malignant disease.

1. Preliminary treatment in cases suitable for operation.
2. Post-operative treatment of the seat of operation and areas of possible extension, i.e., careful and repeated exposures of the areas drained by the lymphatics originating in the area of disease.
3. Treatment of recurrent growths.
4. Treatment of inoperable cases and recurrences of considerable size.

1. Preliminary Treatment.—Under heading 1 we take into consideration all cases of malignant disease, particularly when the disease originates in an accessible region. When time permits, a number of X-ray exposures should be given at regular intervals. Recognising in these cases that operation is imperative, one would not suggest any delay in operating in order that X-ray treatment should be carried out, but in the few days between diagnosis and operation a few exposures might be given. In carcinoma of the breast, to take a common example, the treatment should be commenced as soon as the disease is recognised. A full exposure should be made over the affected area and its surrounding parts; the axilla should at once get a full pastille dose. The special advantage of the latter treatment will be recognised when we state that such an exposure will result in the complete epilation of all the axillary hair in about three weeks from the date of exposure; further, a certain degree of atrophy will take place in the sweat glands of the axilla. Where time permits a second filtered dose may

* Communicated to the Medico-Chirurgical Society of Edinburgh, 2nd February 1921.
be given at the end of a week. As a rule, the result of the two exposures will be a complete epilation of the axillary hair and a marked degree of atrophy in the sweat glands. Should the patient be operated upon a week after the commencement of treatment, by the time the stitches are taken out—i.e., in ten to fourteen days—the condition of the axilla will be as follows: (1) hair in axilla nearly completely epilated; and (2) sweat glands undergoing atrophy. Result, diminution of the sweating in axilla, removal of hairs, and a considerable improvement in the comfort of the patient. In the majority of breast operations the discomfort of the patient from irritation of hair and accumulation of sweat in the dressings is considerable. The advantage of a clean axilla after operation should be of importance in the after-treatment. Further, the irradiation of the whole area of lymphatic drainage should help to prevent recurrence in the line of scar and stitch wounds.

2. Post-operative X-ray Treatment of Area of Wounds and Lymphatic Drainage.—This should be thorough and systematic, and should cover the breast, axillary, and supraclavicular regions. Treatment should be undertaken as soon as possible after the operation; it may be carried out without disturbing the dressings. An exposure once a week for the first month may be given, and thereafter once every three weeks for several months.

3 and 4. Treatment of Recurrent Nodules and inoperable cases.—The majority of the cases of malignant disease which come for X-ray treatment come under these classes. Many of these cases are quite hopeless from any point of view so far as cure is concerned, yet the relief of pain in many cases is marked. Early recurrence yields to repeated X-ray exposure. The routine treatment is to expose the area to X-rays at least once a week, and with filtration similar to that described under post-operative treatment. Treatment is kept up until a marked reaction is obtained over the whole area. Should the reaction be excessive the treatment may be suspended for a month and resumed at the end of that time. Under a régime of this kind nodules disappear gradually, pain is relieved, and the patient improves in general health. After the nodules have disappeared treatment should be continued at intervals of three weeks for at least a year, and after that should it be considered necessary.

An experience in the treatment of cancer by X-rays and
Robert Knox

radium extending over nearly twenty years has led one to the following conclusions: (1) Early recurrence in slowly growing types of carcinoma is particularly amenable to X-ray treatment (many cases show marked improvement; in others the nodules disappear and the enlarged glands slowly subside); (2) larger ulcerated areas slowly heal and leave a sound scar (several of these cases have remained healed for years); and (3) inoperable cases may by means of treatment be rendered operable. Some cases of carcinoma do not yield to X-rays or radium treatment. The explanation of the causes of failure is difficult. When the growth occurs in subjects under thirty-five years of age the prognosis is always grave; such cases recur early and do not yield to X-ray treatment; the masses slowly increase in size and the patient dies from exhaustion; other cases respond at first to treatment, then after a time the growth appears to get the upper hand and rapidly spreads. Occasionally treatment seems only to stimulate the progress of the growth; this may be due to insufficient dosage, though in several cases of this kind I have pushed the dose to the maximum degree without any apparent beneficial result.

One is frequently met with the argument that there is no conclusive proof that X-ray treatment after operation prevents the recurrence of the growth. It is no proof in any particular case which has had X-ray treatment and has not shown recurrence for years that the X-ray treatment really ensured the non-appearance of the growth. I have seen many cases of cancer years after operation with no sign of recurrence. These patients received no after-treatment. How, then, can we prove the value of post-operative X-ray treatment? It can only be done with the co-operation of the operating surgeons. Careful statistics of all the cases operated upon must be kept; two groups of such statistics must be considered. First you must ascertain the percentage of recurrence and period of recurrence in a group of cases which have not had any after-treatment. The second group should be those which have had X-ray treatment. A comparison of the two groups should enable us to ascertain definitely the value of X-ray treatment. Not only must the percentage of recurrence be taken into consideration, but any prolongation of the interval of time which elapses between the operation and the recurrence should be considered in order to aid us in our attempt to assess the value of X-rays in treatment. Should the percentage of recurrence show a
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marked fall, then the distinct advantage of X-ray treatment must be admitted.

When considering the value of X-ray treatment for actual recurrence we can definitely state that X-rays do cure such cases, sometimes permanently, or at all events for a period extending into years. This fact, to my mind, is a valuable one in favour of the plea for the systematic treatment of all cases of cancer after surgical operation. If by X-rays we can cure cases of actual recurrence, surely it is a logical conclusion at which we arrive to state that in all probability we can prevent the actual recurrence if treatment is pushed vigorously immediately after operation. Let us consider the method by which the cancer propagates itself in cases which have been operated upon. The commonest seat for recurrence is in (1) the scar; (2) stitch infection; (3) the outlying tissues where the growth has been left in small portions, or it may be (4) cancer cells which have been squeezed out of the mass at the time of operation; and (5) lymphatic extension. The glands may not have been completely removed. Presuming that any one of these cases is operative we commence at once to irradiate the whole area and surrounding tissue. Inflammatory action is set up all over the tissues irradiated, fibrous tissue formation results, the cancer cells are involved in the general fibrosis, and are rendered harmless. The process which we know to be effective in the treatment of actual recurrence must a priori be beneficial in treating cases which, in a certain percentage at least, must show recurrence.

Estimation of the value of X-rays and radium in the treatment of malignant disease, with special reference to Breast Carcinoma and Carcinoma of the Uterus.—This can only be dealt with briefly. I have already indicated the technique of the treatment in carcinoma generally. The study of carcinoma of the breast has been an extensive one, and it is evident that we owe a great deal to the pioneer worker, Sir Harold Stiles, and to Mr Sampson Handley who has demonstrated the spread of cancer by permeation. If we bear the work of these two surgeons in mind we are materially helped in our appreciation of the extent of the spread in this disease, and are clearly shown that the treatment must be very thorough if we are to hope for a successful result.

There can be no doubt of the value of the post-operative treatment by X-rays. It certainly should be a routine treatment.
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In breast carcinoma it is equally certain that the operative treatment should in all cases have the first choice, and no case however favourable it may be, should be submitted to radiations until the advantages of the operation have been explained.

It is equally important that the need for thorough irradiation treatment should be pointed out to the patient and the object for which it is used explained. Surgeons are adopting this method more generally, and it is especially insisted upon by Mr Sampson Handley in a recent paper published in the Lancet. He is also adopting the method of using radium at the operation, and claims that it has a distinct advantage in preventing recurrence.

In inoperable carcinoma radiation treatment may render the condition operable at a later day; the possibility of this should always be kept in view when treating these cases.

The position is somewhat different when dealing with uterine carcinoma, when the operative results are perhaps not so favourable as in breast carcinoma. X-rays and radium, and particularly the latter, are challenging the operative method, and in the extensive cases offer as much chance of success. Radium when properly used gives excellent local results. Carcinoma of the cervix uteri, for instance, may completely disappear after radium has been applied. The local symptoms disappear and the patient improves greatly in health. The local disappearance of the growth is, however, not a cure; the disease has infiltrated deeply into the pelvic lymphatics. Radium does not appear to check these deeper manifestations any more than the most thorough operative procedure succeeds in removing the more distant deposits of new growth cells. Radium applied internally and X-rays externally appear to offer the best chance of a cure in these desperate cases. The X-rays may in the future acquire a greater utility when more penetrating rays and much larger doses are used.

When the operative method is given the preference the patient should be advised to submit to X-ray treatment in the hope that the deeper involvements may be kept in check. I feel convinced that it is only by whole-hearted co-operation between clinicians, surgeons, and radiologists that the best results can be obtained, and that such co-operation is the best we can do for the patient.

It has been shown that the more malignant types of new growth when superficially placed are influenced by radiations.
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when these are applied in the proper dosage. It may require a very penetrating ray even in the most superficial lesion to bring about the disappearance of the growth. When the growth is particularly resistant to treatment, I believe it is more a question of the quantity of the particular wave-length than actually the wave-length itself. Thus, if a very hard radiation is required, a relatively heavier dose of a softer radiation may bring about the same result.

Some authorities, for instance, state that radium rays are more suitable that X-rays—basing their conclusions on clinical observations. Even in deep-seated lesions X-rays, when used in the correct dosage, will induce the same changes as radium does when buried in a deep tumour. I have seen large masses of peritoneal growth disappear when very large doses of X-rays were administered through several ports of entry through the abdominal walls.* The case of Bailey is another example of the type of case in which the effect can be produced by either X-rays or radium with equal certainty. The great advantage radium possesses over X-rays is chiefly one of practical application.

As already stated, the advantages that radium possesses over X-rays are (1) the shorter wave-length of the gamma ray—and its greater penetrative power; (2) the convenience of its application in certain diseases whose site is in the interior of the body. Until very large quantities of radium are available it is more convenient to endeavour to obtain as good results with X-rays. The penetrative value must be greatly increased by increasing the power of the generating apparatus. Special tubes are required, capable of standing up to the high voltages required to produce the long spark length, and the rays must be applied in a way which makes it possible to concentrate the dose on any particular depth of tissue. All these requirements are capable of accomplishment. The apparatus has only to be specified. It is possible to make it. The tubes are already available. The actual application is not difficult. The “cross-fire” technique is well known. It consists of a number of ports of entry, the rays being centred on a particular spot from each of these ports. Mechanical contrivances are readily made which facilitate the execution of a technique of this kind.

The rotating tube is capable of administering with great

* Recent works published in Germany appear to support this view.

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accuracy a large dose of X-rays at a particular depth of tissue; if X-rays are employed in this way it is possible to administer in several hours as large a dose of radiation as could be obtained from a very large quantity of radium buried in the tumour for a day or two. The advantage X-rays possess when employed in this manner is that no operative measures are required—often a point of some importance.

To take an example. Suppose that a case of epithelioma of the skin has been successfully treated by X-rays and radium, and the dose is approximately X.

The lesion being on the surface receives 100 per cent. of the beam of radiations directed upon it.

The absorption value of the particular wave-length is ascertained, and is as follows:

1 inch of tissue absorbs, say, 50 per cent.
2 " " " 75 "
3 " " " 85 "
4 " " " 95 "

To produce the same effect upon a tumour of similar type at say 4 inches depth from the surface will take twenty doses from as many ports of entry, as only 5 per cent. of the beam is absorbed in that depth. If the skin dose take 15 minutes then the depth dose will take $15 \times 20 = 300$ minutes or 5 hours.

When the penetrative value of the radiation is increased the absorption by the intervening tissues diminishes, and it may be possible to project 20 per cent. of the beam 4 inches into the tissues, when the 300 minutes would be diminished to 75 minutes. It is possible when using these very penetrating rays to utilise the same skin area for three or four doses; in this way the number of ports may be diminished.

Conclusions.—It follows from what has been said that in X-rays and radium we possess most useful agents, and that extensive use should be made of these in the treatment of a large number of diseases. The value of such treatment will depend upon several factors.

(1) The time at which it should be administered.
(2) The nature and extent of the disease.
(3) The response the tissues possess to stimulation. Many patients are reduced to the last point of resistance before they are treated. These cases fail to respond.
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(4) The dosage, which may be

(a) Massive at one sitting or divided over several days.

(b) Intermittent, large doses being given at intervals of from one to six weeks.

The malignant cases give the least favourable results. The earlier a case can be treated the greater is the chance of a successful result. Surgery offers in nearly all cases a better prospect than radiation treatment, so it should be given in the first place, and radiation should be used after operation in the hope that recurrence may be delayed or prevented. Combined treatment should be more successful than either alone.

There are conditions of malignant disease in which surgery may not offer any better prospect than radiation, and in these it should be our aim to give the very best treatment in the hope of helping the patient. Radiations must be very thoroughly administered. In malignant disease of the thyroid, for example, it may be possible to do as much with radiation as by surgical operation. Large tumours of a low degree of malignancy may be diminished in size and their progress delayed.

In conclusion, I wish to show you slides from a case of mediastinal tumour which reflects great credit upon those who dealt with the case, and shows how advantage was taken of the therapeutic action of radium and X-rays.

The slides I show explain the nature of the tumour and its exact position in the thorax. Through the localisation of the tumour by radiograms taken in three positions, the surgeon was able to operate by opening the anterior chest wall. Excellent judgment was shown in the administration of the radium dosage, where the tubes of radium were inserted in the mass of the growth. Subsequent exposures to X-rays resulted, a year after treatment, in the production of the condition I show in the next slide. The case did remarkably well, and furnishes a most striking testimony of the great value of Rontgen's discovery of the X-rays, and the subsequent developments in the technique of diagnosis and treatment. It is a fitting illustration of the best method, i.e., collaboration of the physician, the surgeon, and the radiologist.