Medical.

THE INDICATIONS FOR TREATMENT BY X-RAYS.¹

BY WALTER M. LEVITT, M.B., M.R.C.P., D.M.R.E.

Medical Officer in Charge of the Radiotherapeutic Department, St. Bartholomew's Hospital.

IN setting out this short article it has been my aim to avoid technical details and to regard the subject from the point of view of the post-graduate who seeks information as to the utility of deep X-ray therapy in his practice. Looked at from this aspect the first desideratum is to provide some guidance in the selection of suitable cases. Secondly, to indicate what may be expected from these cases under treatment, not only as regards the ultimate results, but also regarding what we might term the debit side of the account, namely, the nature and extent of the ordeal to which the patient is to be submitted during treatment, and any risks that may be run.

Obviously any discussion of technical details would be out of place here, but it may be of interest to indicate in general terms, so far as we know them, the manner in which the rays act in the diverse conditions with which we shall have to deal.

Before embarking upon the main task I want to make it clear that I shall endeavour to present those particular aspects of X-ray therapy with which we are concerned in a manner which is as "cut and dried" as possible, in order that it may be easy to follow and perhaps to remember. I can only claim to expound the position as I, and I believe many of my colleagues at St. Bartholomew's, see it. I have no doubt that there are many people of standing who would disagree with some of my statements. This difference of opinion, however, is not unnatural when we come to consider that X-ray therapy is still a comparatively new science and a very complex one, making as it does contacts with so many other and diverse branches of science—physics, chemistry, engineering, biology, pathology, medicine and surgery, to mention only a few of the closer contacts. Hence it may seem that the claims I put forward for X-ray therapy are but moderate, but to my mind the science still being in its adolescence, this is erring in the right direction.

In attempting to cover such a large field in a brief space of time it will be well to adopt some sort of classification of the various conditions we shall discuss.

In the first place I propose to consider the conditions which are treated by X-rays

¹ Based on an address read upon the opening of the new X-ray, X-ray Therapy and Urological Departments of the Derbyshire Royal Infirmary, May 26, 1932.

under two main headings : non-malignant and malignant. We shall deal with the non-malignant conditions first.

The NON-MALIGNANT conditions which may be treated by X-rays can be classified as follows :—

- (1) Various diseases of the skin, including keloid and contracted scars.
- (2) Certain chronic inflammatory conditions, simple and tuberculous. This group may be further subdivided as follows : (a) chronic enlargement of lymphatic glands, usually tuberculous ; (b) tuberculosis of the larynx ; (c) tuberculous peritonitis ; (d) certain forms of chronic arthritis ; (e) the earlier stages of simple enlargement of the prostate.
- (3) Chronic leukæmias.
- (4) Lymphadenoma.
- (5) Hyperthyroidism.
- (6) Certain gynæcological conditions.
- (7) Chronic mastitis.
- (8) Parotid cysts and fistulæ.

Diseases of the Skin. The treatment of these conditions, with the exceptions, perhaps, of keloids and lupus, usually falls to the lot of the dermatologist to carry out, and I shall only refer to them very briefly here.

In general, it may be said that it is the more chronic diseases of the skin that are most benefited by X-ray treatment, and, indeed, during the acute stages X-ray treatment is usually contra-indicated.

Among the conditions that are most benefited are tinea of the scalp, chronic eczema, psoriasis, sycosis, lupus vulgaris, and keloids.

With the exception of ringworm and perhaps keloids, in none of these conditions can X-rays be described as a sovereign remedy, although they often secure a measure of relief which is not afforded by any other method of treatment.

The X-ray treatment of ringworm and also of sycosis involves complete depilation of the affected areas. In the case of the former condition this is easy to secure, and in reliable hands is without danger. In sycosis, however, dosage sufficient to induce epilation is sometimes precluded by the acuteness of the condition. In such cases the prospect of benefit with X-ray treatment is greatly reduced.

In chronic eczema, and also in psoriasis, although many cases are greatly benefited, recurrence is the rule rather than the exception.

In lupus, whether involving skin or mucous membrane, the results are good, and X-ray treatment offers many advantages over the Finsen and similar methods in this disease.

The favourable effect of radiations on keloids is well known, and, indeed, alone or combined with excision, it is the only satisfactory method of treatment of this condition.

Keloids. Treatment, as a rule, takes the form of single exposures with heavy dosage, strictly localized to the keloid, with intervals of a few weeks. Usually two or three exposures are sufficient, except in the case of very extensive keloids, which are better treated a portion at a time. No ill-effects at all should follow the treatment. Improvement should be manifest within three weeks, and usually continues for as many months. The rays probably act by causing obliteration of blood-vessels—a well-known effect which is easy to demonstrate experimentally.

In all other dermatological conditions, with the exceptions of ringworm and sycosis, dosage is small, and the general reactions produced but slight. Local reactions of varying degree are to be expected, and occasionally are severe. Such severe reactions are usually to be regarded as evidence of hypersensitivity of the affected skin to radiations, and can usually be avoided by reducing dosage in subsequent treatments.

As regards the treatment of glandular enlargements, usually of tuberculous origin, this will vary with the condition of the glands. Long-standing enlargements which show no evidence of breaking down are best treated by fairly small weekly doses of moderately hard rays for six to eight weeks, and the results are excellent.

Larger doses may lead to a quicker result, and may save the patient a certain number of exposures, but they involve the risk that the glands may break down.

Glands which are more acute in character, or show a tendency to breaking down, have to be given still smaller doses at weekly, or slightly shorter, intervals over a longer period. An exceedingly important point is, that whenever fluctuation is detected the glands should be aspirated under the most stringent aseptic conditions. They should never be allowed to discharge spontaneously if this can possibly be avoided, and it is common experience for a mass, which has had to be aspirated on several occasions, to disappear without a sinus, or, indeed, without a trace of their presence being left on the surface.

In this, as in other chronic inflammatory conditions, the chronicity of the process is due, or at any rate contributed to, by the packing of the tissue spaces with the small round cells, which are characteristic of chronic inflammation. Now the leucocytes are among the most sensitive cells in the body to radiations. In fact, a blood-count on any patient who has had intensive irradiation invariably shows a leucopenia which may persist for weeks. It is therefore reasonable to suppose that the rays act by destroying many of the cells which pack the interstices of the gland, thus inducing an increased circulation through the gland, and an inflammatory reaction depending in intensity upon the dosage applied. In fact, therefore, what we do by our X-ray treatment is to induce and keep up an inflammatory reaction of a grade which can be controlled by the dosage, so that the tuberculous or other infective process is dealt with by the tissues much more energetically than it otherwise would be. The after-effects of the treatment are negligible. Many of the patients treated at St. Bartholomew's hurry into the Hospital for their treatment during their luncheon interval from work, and return to their work immediately after the treatment.

The same remarks apply to the other tuberculous conditions mentioned.

X-rays are frequently recommended for the treatment of chronic arthritis. Except in the case of spondylitis, where occasionally remarkable results are seen, I, personally, have had little success in the treatment of these conditions.

I would not advise the treatment of prostatic hypertrophy by X-rays except in the early stages, before the urine has become infected, and even then only in the presence of some contra-indication to operation. Only when large doses are applied are successes obtained, and such doses, unless in skilled hands, are not free from danger. It should be said, however, that with hard rays and correct technique irradiation does not render subsequent operation more

Enlarged Prostate.

difficult. A certain amount of sickness, perhaps diarrhoea and general malaise, are to be expected in association with the treatment of this condition.

The use of X-rays in the treatment of this disease, or rather group of diseases, is practically confined to the more chronic types. Except for palliative purposes in the

Leukæmia. relief of urgent pressure symptoms, for example, greatly enlarged cervical glands pressing on the trachea, X-rays have no place in the treatment of acute leukæmia.

Much has been written on the X-ray treatment of leukæmia during the past twenty years, yet I venture to suggest that the position with regard to the X-ray treatment of this condition has not improved a great deal since the early days of X-ray therapy. We have, perhaps, learned to recognize and to guard against some of the dangers of the treatment. With greater certainty of dosage, our treatment is under more exact control, and we can therefore, as a result of our irradiation, and without undue danger, bring the patient to a state more closely approaching normality. He therefore feels better and is able to go about his work more efficiently for the greater part of the span of life that remains to him. On the other hand I do not think that on the whole life is greatly prolonged. You may say then, why treat the patient at all? The answer to this question is that although the *duration* of life is not prolonged, its *quality* is much improved by the X-ray treatment. Thus the patient who, without X-rays, would be doomed to spend the greater part of the remaining months or years of his life in his bed is, as result of X-ray treatment, restored to fair comfort and ability to work until quite shortly before the end.

The X-ray treatment of leukæmia is best applied as a short semi-intensive course, with the object of reducing the white count to from 8,000 to 10,000 per c.mm. It is found that it is only when the white cells are reduced to this level that the longest remissions are secured. On the other hand, experience and judgment are required if the leucocyte count is to be brought as low as this without undue danger. It should be remembered also, that the count continues to fall for two or three weeks after the X-ray treatment has been completed, and therefore treatment is usually stopped when the white count has fallen to from 15,000 to 20,000.

Equally important, with the white count as a guide in controlling the X-ray treatment, is the behaviour of the red cells and hæmoglobin. If these rise, the immediate prognosis is good, and *per contra*, if they fall during treatment the prognosis is bad. First, remissions in favourable cases last for from several months to two years, or even longer. The duration shortens with successive remissions.

The mode of action of X-rays in leukæmia is not understood. In my experience, the best results are obtained when the rays are applied to the spleen only, and the effect is probably by means of some leucocyte destructive agent produced by the action of X-rays on the spleen.

Here again we have to deal with a disease which, although incurable, is greatly relieved by X-ray treatment. Not only can local swellings be made to disappear wherever they arise, but the peculiar toxæmia associated with the disease

Lymph-adenoma. can be held in check for a longer or shorter time. Ultimately, however, extensive abdominal and thoracic deposits appear and herald the end. Abdominal deposits tend to be very radio-resistant, and make the outlook very grave.

The average duration of lymphadenoma with X-ray treatment is a few years after

coming under observation, but it is not uncommon for cases to go on for eight, ten, or even twelve years.

These are most easily discussed if we classify uterine hæmorrhage due to causes other than malignant disease, with special reference to the mode of treatment under consideration.

Gynæcological Conditions.

We may first subdivide the causes of uterine hæmorrhage into functional and organic. Functional hæmorrhage occurs at two epochs—puberty and the menopause. Except in cases of such gravity that life is threatened, X-ray treatment should not be employed in the hæmorrhage of puberty. However, in cases of sufficient gravity, X-ray treatment is always to be preferred to hysterectomy, since the sterility induced by X-rays in such cases is only temporary, persisting at most for a few years. Moderate doses only are required, and the action induced by the treatment is not severe.

In functional menopausal hæmorrhage, on the other hand, X-ray treatment is the treatment of choice, the results are swift and certain, and the after-effects transient and of little account.

As regards the hæmorrhages of organic origin, these may be due to a variety of causes, although the greater number are associated with the presence of fibroids. Time does not permit of a consideration of these conditions in detail, but it is possible to make certain generalizations which apply to all of them.

In the first place X-rays should not be employed in the treatment of non-malignant pelvic disease in the female in the child-bearing age. There are a few—a very few exceptions to this rule. Only when the disease is so extensive as to preclude any possibility of a future pregnancy, when it is progressive (for example, advanced pelvic tuberculosis), so as to threaten life, when no other treatment is possible, and when there is a reasonable chance of X-rays doing good, is it justifiable to apply X-ray treatment in women under 40 years of age. Between that age and the menopause the contra-indications may be somewhat relaxed, but under the age of 45 such treatment should not be applied without careful consideration.

Although temporary sterilization, with subsequent complete recovery of function, can be carried out in patients under 40, and is often recommended in the treatment of various conditions, I do not think it is justifiable, except in the presence of one or other of the indications referred to.

The term chronic mastitis probably includes a variety of conditions of differing nature and ætiology. The old teaching that these conditions predisposed to carcinoma is now regarded with doubt, and it is probable that the truth is that certain varieties of chronic mastitis, forming, however,

Chronic Mastitis.

only a small proportion of all cases, are to be regarded as pre-cancerous conditions.

A large proportion of cases of chronic mastitis responds well to X-ray treatment, and only quite small doses are necessary. It is not improbable that the cases that fail to respond to such small doses are of the type which tends to develop carcinoma. I would, therefore, urge that operation should be carried out in cases which prove resistant to X-rays.

With increasing use of radium in the treatment of carcinoma of the breast, and in view of the possibility that carcinoma may develop later in chronic mastitis, it behoves the radiologist to use every effort to avoid causing radiation changes in the healthy tissues. These considerations have led, or rather should lead, to considerable revision

in the method of X-ray treatment of chronic mastitis, and the scrapping of the older methods. Thus, a not uncommon method of treatment in the past has been with the use of soft (non-penetrating), even unfiltered rays, so that only an extremely small fraction of the dosage applied to the skin could reach the deeper portions of the breast. In order, therefore, to obtain the desired result, quite large doses had to be applied to the skin, and permanent changes were consequently induced.

By the use of penetrating radiations dosage can be kept low, and the danger of radiation change in the healthy tissues is obviated. Fairly powerful apparatus and high filtration are necessary to achieve these objects.

Treatment is usually applied weekly for four to six weeks, and improvement should be quickly manifest. No general reactions are produced, but occasionally local swelling and tenderness are observed for a day or two after treatment.

This is a condition which, as you know, is frequently treated by X-rays, and we find that the most diverse opinions are expressed as to the value of this form of treatment.

Hyper-thyroidism. This may be due in part to the diversity of techniques which are employed by radiologists in the treatment. I do not think, however, that this factor can entirely account for the differences of opinion; a more probable explanation is that the interpretation placed upon the term "successful result" varies with different observers.

I may say, straight away, that if by the term "successful result" you mean a complete abolition of all symptoms and signs of the disease, the percentage of successes is small indeed. That improvement of some degree with X-ray treatment is the rule rather than the exception is, I think, indisputable, and in a proportion of cases the abolition of symptoms may be almost complete. Even in the most successful cases, however, exophthalmos rarely disappears.

An important point to be remembered is that in a case in which cardiac affection renders an operation undesirable X-ray treatment may cause sufficient improvement greatly to diminish the surgical risks. With modern methods of X-ray treatment operation is not rendered more difficult or more dangerous.

The treatment of exophthalmic goitre is usually carried out by means of small doses administered at intervals of several days—usually for convenience once weekly. The patient will then have to attend for from six to nine weekly doses, and the series may have to be repeated after several months. Improvement may continue for many months after a single series.

The after-effects of X-ray treatment of hyperthyroidism are slight, but the possibility of telangiectases and other skin changes at a later date, perhaps after an interval of years, should not be overlooked. Experience has shown that the skin of hyperthyroid patients is often unduly sensitive to X-rays. However, with modern high-powered apparatus even this risk is minimized, since the rays are sufficiently penetrating to enable adequate dosage to be obtained in the depths of the thyroid gland, however enlarged, without undue irradiation of the skin.

The last in the list of non-malignant conditions I gave you were parotid cysts and fistulæ. You may think that these are such rare conditions as not to merit mention in a brief survey of this sort. However, when they occur they cause such misery and suffering to the patient—in the case of parotid cysts the patient may actually starve because eating is associated with intolerable pain—and the effects of X-rays are so

certain that I think they are worth mentioning. It so happens that the salivary glands, especially the parotids, are very radio-sensitive organs, and can be destroyed by a single properly judged dose of X-rays, and this is of course how the therapeutic effect is produced in these conditions.

Malignant Disease. So much has been written on the X-ray treatment of malignant disease in the last few years, that I do not propose at this stage to weary you with anything more than the very briefest summary of the position.

We shall consider malignant disease in relation to X-ray treatment under three main headings, namely, carcinoma, sarcoma, and endothelioma.

This is a classification which, as you see, rests mainly on a histological basis. Although, broadly speaking, radio-sensitivity is different in these three groups, when we try to pursue a histological classification a little further with the object of seeking a guide to prognosis, we find that in most cases histology proves a broken reed upon which to lean. You will often see it stated that squamous-celled carcinoma is radio-sensitive, spheroidal-celled carcinoma is less sensitive, and columnar-celled carcinoma is insensitive. Such generalizations are incorrect and misleading. In my experience the radio-sensitivity of a carcinoma is determined to a much greater extent by its site of origin than by its histological characters. To take an example, carcinoma of the palate and carcinoma of the tonsil are both squamous-celled growths, they arise in similar epithelium, and their histological characteristics are similar. Yet, carcinoma of the palate is one of the most radio-sensitive carcinomata with which we have to deal, while carcinoma of the tonsil is one of the most radio-resistant. Similarly carcinoma of the rectum and carcinoma of the body of the uterus are both columnar-celled growths, yet the former is extremely radio-resistant and the latter is fairly radio-sensitive.

On the whole rapidly growing tumours are more radio-sensitive than slow-growing ones, but even this statement is not universally applicable. Thus an extremely chronic scirrhus carcinoma of the breast may contrary to all expectations melt away upon the application of X-rays.

The point I want to make is, that while there are a few situations in which we know that carcinoma tends to be radio-sensitive, in the large proportion of cases a prognosis is not possible until the behaviour of the tumour under irradiation can be observed.

Among the more radio-sensitive growths are all skin carcinomata, carcinoma of the cervix, carcinoma of the palate, carcinomata arising in the post-nasal space, carcinoma of the uterine body, postcricoid carcinoma. The seminal epithelioma of the testis is one of the most sensitive growths known, and if this fact is not recognized serious results may follow the administration of ordinary doses in this variety of carcinoma. I have known a severe toxæmia follow within a few hours of the application of a quite moderate dose to a seminoma. In that short interval the reduction in size of an enormous growth was so remarkable that it could only be supposed that toxæmia was due to absorption of disintegration products.

Finally, in connection with carcinomata, cases not suitable for X-ray treatment are: carcinoma of the stomach, most carcinomata of the œsophagus, carcinoma of the liver, extensive carcinomata of the lung. Any carcinoma which has become generalized should not be treated by X-rays. Carcinomata in the throat associated with the presence of very hard fixed glands are also unsuitable.

As regards the sarcomata, here the histological characters afford us a little more

assistance. Small round-celled sarcomata are extremely radio-sensitive, and can almost invariably be made to disappear. In these, it might almost be said that the decisive factor in the result of treatment is the presence or absence of secondary deposits. *Per contra* death in this condition treated by X-rays is nearly always from generalized deposits, and not from the local disease. I have a patient, who over five years ago had a sarcoma of the upper jaw which was successfully treated by X-rays. Some months later she got a deposit involving four ribs, which was also successfully treated. Three years ago she got another secondary deposit in the terminal portion of the ileum, which perforated, and gave rise to peritonitis. She was operated upon, recovered, and was given further X-ray treatment, and has remained perfectly well ever since. She works hard in a factory and does not appear to suffer any inconvenience from her previous experiences. A specimen of the abdominal secondary deposit is in the St. Bartholomew's Hospital Museum.

The other varieties of sarcoma vary greatly in sensitivity, the most resistant being the mature forms of fibro-sarcoma. Melanotic sarcoma, contrary to what might be expected, is a resistant growth, and one the treatment of which is not without danger from the occurrence of severe local and general reaction.

The endotheliomata are again very variable in their radio-sensitivity. The mixed parotid tumour is radio-resistant, while the endotheliomata occurring in the throat are often highly radio-sensitive.

As regards the actual X-ray treatment of malignant disease, the best results can only be obtained when high-powered apparatus is available, and when intensive methods of treatment are used. Reactions are often severe, both general and local. Thus a certain amount of vomiting, lassitude and anorexia are almost inseparable from the treatment of any extensive malignant lesion, and while local reactions in the form of erythemata of skin and mucous membrane associated with discomfort and soreness are to be expected, it cannot be too strongly emphasized that true X-ray burns should not occur. Any radiologist who states that intensive X-ray treatment is not justifiable because of the danger of burns, is self-confessedly a poor X-ray therapeutic technician.