A Lecture ON THE TREATMENT OF MALIGNANT DISEASE OF THE SKIN.*

BY J. H. SEQUEIRA, M.D., F.R.C.P., F.R.C.S.,

PHYSICIAN TO THE SKIN DEPARTMENT AND LECTURER ON DERMATOLOGY
AT THE LONDON HOSPITAL; CONSULTING DERMATOLOGIST
TO THE RADIUM INSTITUTE.

I PROPOSE first to consider shortly the varieties of cutaneous malignant diseases and to indicate certain special features in each which have a special bearing upon treatment.

CARCINOMA.

As elsewhere, we may divide our cases into those in which the malignant process develops in the epiblastic layers and those which are mesoblastic in origin. Of the former we have four varieties of carcinoma:

1. Squamous or horny-celled carcinoma, so-called "epithelioma."
2. Basal and glandular-celled carcinoma, which include most of the cases known as rodent ulcer.
3. Naevus-carcinoma (cancer developing in naevoid growths, moles, etc.).
4. Paget's disease.

The Squamous-celled Carcinoma.

This is characterized histologically by an excessive growth of horny cells of the epidermis with numerous downgrowths into the true skin and subcutaneous tissue, forming the so-called cell nests or epithelial pearls. An important characteristic of these affections is the early involvement of the lymphatic glands and the formation of metastases in the viscera.

Clinically, the squamous-celled epithelioma may be at the onset a small warty excrescence of simple appearance. It may develop upon a senile keratoma, a common warty lesion occurring in the skin of old people. Similar growths follow prolonged exposure to the sun, wind, and weather, and these conditions have been specially studied by Unna, Dubreuilh, and others. Unna described the condition as seen in sailors as "seaman's skin cancer," and Dubreuilh has classed similar conditions due to actinic light as "solar epitheliomatosis." Irritation by x rays acts in a similar manner. Chronic irritation of the skin by tar, paraffin, creosote, and soot may similarly cause squamous-celled carcinomata. In all these conditions we find pigmentation, small warty excrescences, and these may finally become malignant. Lastly, we may find them upon the cicatrices of lupus vulgaris, lupus erythematosus, syphilis, and, in fact, on many kinds of scar tissue.

The squamous-celled carcinoma is most commonly met with on the face, especially about the orifices, the lips especially, and on the backs of the hands; but it may occur anywhere. The warty growth remains inconspicuous for some time, and causes no pain or discomfort, and usually the patient takes little or no notice of it. Then, as the result of some irritation, or for some unknown cause, it starts growing, and becomes deeply attached, and it may develop into a larger tumour, or a button-like excrescence, and sooner or later break into an ulcer with everted edges. Early in the course of the case, as a rule, the nearest lymphatic glands become hard, tender, and painful. The essential point to remember in treatment is that the squamous celled growths invade the glands early.

Besides the warty growths which we have just considered, there is a form of epithelioma which is nodular. This occurs on the lips and mucous membrane of the mouth, and on the external genitals. The lesion runs a slow course, but ultimately infiltrates. A deeply spreading highly malignant variety especially occurs at the mucocutaneous junctions. The tumour rapidly increases in depth, speedily involves the lymphatic glands, and may cause death by the involving of large blood vessels.

Baso-Cellular and Glandular Type; Rodent Ulcer.

In this important group the neoplasm arises from the deep or basal layer of the epidermis, and from the sebaceous ducts and hair follicles. On the Continent and

in America the term "epithelioma" is applied to these conditions, but in this country the name "rodent ulcer" is most commonly used. The tumours consist of processes which invade the true skin and subcutaneous tissue in the form of lobules. The processes and lobules are composed of cells which have either the character of the basal cells of the epidermis or cells which line the pilo-sebaceous ducts. The essential feature of this type of lesion is that the lymphatic glands are rarely, if ever, involved. The primary lesion is usually a firm nodule of a grey or pearly colour; it often resembles a flat wart, and causes no symptoms. It is frequently unnoticed until the top is cut off in shaving or rubbed off with a towel, when there is a little haemorrhage. The nodule increases very slowly, and then the centre ulcerates and a small crust appears. The progress is very slow, although exceptionally there may be rapid extension with the formation of small cysts.

Clinically there are several varieties:

1. The type in which the ulcer cicatrizes spontaneously in the centre and spreads with a pearly, beaded rim.
2. In this type the ulcer never heals, but spreads slowly and superficially, and also deeply.
3. In the type called "terebant," which may succeed one of the varieties already mentioned, the destruction is extremely rapid and spreads deeply, producing huge cavities with a foul discharge.

Occasionally rodent ulcers are multiple. It is important to remember that the curability of these lesions depends upon the involvement of cartilage and bone, and, provided there are no deep attachments, we can usually promise a cure by the means which are now at our disposal.

Naevus-Carcinoma.

This name is applied to malignant growths developing from naevi. The tumours are usually melanotic, but occasionally are non-pigmented.

Moles, particularly of the pigmented variety, are liable to undergo malignant changes in adult life and in advanced age. Such a tumour may develop with great rapidity, forming a brown or black plaque or warty growth. This may become indurated, and eventually may undergo ulceration. New lesions sometimes appear round the primary tumour, and metastases in the viscera are very common.

Paget's Disease.

The last variety of malignant disease to which I wish to draw your attention is that associated with the name of the late Sir James Paget, and called "Paget's disease." It is important to remember that this condition, which at its onset may resemble a chronic eczema, is a malignant affection *ad initio*. As is well known, it is most common in women over 40 years of age, and develops round the nipple. At first it appears to be an innocent though chronic affection, but very early in most instances there is involvement of the tissues of the breast in the form of duct cancer.

In rare instances Paget's disease occurs in other regions—in the perineum, the external genitals, and at the umbilicus.

TREATMENT.

I have deemed it necessary to insist on the essential differences of these types of malignant disease of the skin, because upon them depend the methods to be adopted in treatment. To obtain success an early diagnosis is imperative, and I would lay it down as a rule that every warty or superficial growth, especially in elderly subjects, should be suspect, and if one has not the opportunity of making a microscopical examination, the condition should be treated as if it were malignant. The measures at our disposal for the treatment of malignant disease of the skin are:

- (a) Excision; (b) radio therapy; (c) radium therapy; (d) diathermy; (e) freezing by carbon dioxide snow.

These measures are undertaken for the removal or destruction of neoplasm and the glands if affected. If we are unable to ensure this, our measures are purely palliative—namely, for the relief of pain and prevention of sepsis.

(a) Excision.

The surgical treatment of malignant disease of the skin consists in the complete removal of the growth by the knife or cautery. The complete removal is sometimes

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difficult, and the details of the operation must be left to the surgeon. It is most important to make the incision wide of the growth and to get below it. Excision is the method of choice in squamous-celled cancer, and at the period of the operation or at a subsequent time the enlarged glands should be removed. With a view to preventing recurrence after excision, it is well to give the patient a series of sittings under x rays. Recently Mr. Richard Warren and I have collaborated in the treatment of squamous epithelioma on the back of the hand. The growth, which was a large one, was excised, and the raw surface was then treated by radium on a plate in a manner to be described shortly. The surface of the wound was in a healthy aseptic condition, and was then covered by Mr. Warren with a skin graft. We were somewhat in doubt as to whether the radium reaction might interfere with the graft taken, but the result was most satisfactory, and the hand has remained perfectly sound ever since. A small gland in the axilla was removed at a later date. If it is impossible to bring together the edges of the wound after such an excision, skin grafting, or in some situations a plastic operation, may be used with great advantage.

(b) Radio Therapy.

In 1901 I had the honour of bringing to the notice of the profession the treatment of rodent ulcer by x rays. Early in that year I published a series of cases in which I had observed the histological changes produced by the x rays in the cells of the growth. I found that the malignant cells had a very low resisting power to the rays, that there were destructive changes, and that at the same time the connective tissue was stimulated to activity. Large cavities filled up rapidly and superficial lesions were cured. The only difficulty lay in the treatment of the infiltrated edge. By the combination of surgical measures with radio therapy this difficulty was overcome, and I have for a number of years advocated preliminary curettage of the edge of the growth, followed by a series of x -ray exposures. In some cases it is more convenient to use the knife than the curette. The dose of x rays is measured by the Sabouraud pastille, full pastille doses being given at intervals of from ten to fourteen days. Where there is a deep infiltration much larger doses are given, even up to eight pastille doses at one sitting, but when this is done the parts are screened by a layer of aluminium varying from 0.2 to 4 mm. These filters prevent chronic x -ray ulcer.

One outstanding feature of the x -ray treatment is this, that if a case is going to do well by this method the improvement is shown at once. If the case is resistant to the treatments and they have to be repeated frequently the outlook is unfavourable. The great thing that militates against success is the infiltration of bone and cartilage. When, therefore, rodent ulcer is already adherent to cartilage or bone, the prognosis is usually unsatisfactory, and I advise an early resort to the aid of the surgeon. Some of the most difficult cases we have to deal with are those in which the disease begins at one or other canthus and involves the orbit. Here again the assistance of the surgeon should be sought early and the orbital cavity should be cleared out and if possible grafted.

(c) Radium Therapy.

Small rodent ulcers, and especially those which are freely movable, react remarkably well to radium. This agent has a decided advantage over x rays in certain situations, because it can be more readily applied. This holds particularly in the neighbourhood of the eye or the angle of the nose, and in a few other situations. As far back as 1902 I was using radium for rodent ulcer, and I am showing to-day a photograph of a case cured in 1903, the rodent being on the lower lid. This has remained quite sound ever since, and the deformity of the lid has been repaired by operation. The introduction of plates upon which the radium salt is spread and covered with varnish has enabled us to treat with greater ease a large number of these superficial malignant growths. The duration of the exposure will depend: (1) On the strength of the radium applicator—for instance, at the London Hospital I have two plates each 1 in. square, upon which are spread 30 mg. of the radium salt. With these applicators I can get an intense reaction with two hours'

exposure. Many radium plates are of half this strength, and consequently an exposure double the length is required. (2) Upon the depth of the lesion. Where the infiltration is deep, it is necessary to apply the radium for a much longer time to utilize the gamma rays. To prevent undue damage to the superficial parts by the alpha and lower beta rays we employ a thin filter of lead, which cuts out these less penetrative rays. It may be necessary to apply the radium plate for twenty-four to forty-eight hours. The radium reaction begins in from eight to ten days after exposure. The parts become swollen, red and irritable, and eventually a crust or scale is formed. With a moderate exposure the crust or scab falls off in about three weeks, and the treatment may then be repeated. If a heavy dose has been given without proper screening a radium ulcer develops very similar to the ulcer produced by x -ray treatment. It requires fomentation and dressing with a mild antiseptic ointment, but as a rule it heals in time. I have already mentioned the use of radium after operations, and think there is possibly a large field for such a procedure.

(d) Diathermy.

My colleague, Dr. R. S. Woods, has treated two or three cases of malignant disease of the skin that have failed to yield to the measures already described by diathermy. In one case the result in a deeply attached rodent ulcer has been so far satisfactory, but the procedure requires further experience.

(e) Freezing by Carbon Dioxide Snow.

Several authors have claimed that much can be done for superficial malignant lesions of the skin by the freezing with carbon dioxide snow. I have used it occasionally, and in some quite superficial cases have seen good results, but I have frequently been asked to treat by radium cases in which this method has been used without success.

Treatment of Severe Cases.

Lastly, I have to say a few words about the use of the x rays and other measures in the more severe cases. Even in some of the worst great benefit may be derived from x -ray treatment, as is shown in cases of which I am exhibiting photographs. Care must be taken not to overdo the x -ray treatment, because it is quite possible to stimulate an indolent process to one of greater activity by excessive x -ray treatment. Scrupulous cleanliness and application of antiseptic lotions, such as hydrogen peroxide, mercury, etc., may be necessary to treat the parts when the ulcer is in this sloughing condition.

Treatment of Paget's Disease.

Paget's disease demands a brief statement. I cannot too strongly emphasize the fact that this disease is malignant, and that even when the lesion appears to be quite superficial there is a great possibility that the adjacent breast tissue is already involved. I have seen a case of Sir Malcolm Morris's in which Paget's disease about the umbilicus was healed by radium. I have three times healed up lesions of this type by x rays, but in each of these three cases I regretted the time lost in doing this, for the disease had already involved the glandular structure underlying the healed surface. I therefore advise an early treatment by the removal of the breast and glands, should any be involved.

Other Malignant Diseases.

Of the use of the x rays to some of the other malignant and pseudo-malignant conditions I will again say a few words. For mycosis fungoides the x rays act like a charm upon the tumours and infiltration met with in this disease, but it is impossible to say that they are curative of the condition. In my experience only one case has so far been apparently cured by the rays.

In the rare condition known as the multiple idiopathic haemorrhagic sarcoma of Kaposi I have seen the complete disappearance of the infiltration and growth under the x rays.

Some of the true sarcomata are also benefited, but they are usually so rapidly disseminated that it is impossible to say what more than palliation can be promised.