ROENTGEN RAYS OR RADIUM COMBINED WITH EXCISION IN THE TREATMENT OF KELOIDS *

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Keloids or hypertrophied scars are difficult to treat and require much patience on the part of both patient and physician. So far as is known, the roentgen ray and radium are the only two agents which will arrest the disease or cause it to disappear. If these agents are used early when the scar begins to hypertrophy there will probably be no need of combining excision with the radiotherapeutic effect. It is because of the frequent neglect of hypertrophied or growing scars that it is necessary to call attention to these methods of treatment. If the general practitioner, the surgeon and the dermatologist are alert and apply skilfully the roentgen rays and radium to scars that are beginning to show hypertrophy, keloids will almost be eliminated from the field of medicine. It is true that in many instances slight wounds, especially in the colored race, lead to the formation of large keloids and often these cause so little inconvenience to the patient that they are liable to be neglected until they have reached a considerable size. Too often, however, the surgeon recognizes his helplessness and therefore neglects the condition, and the patient, fearing further deformity from treatment, neglects the condition entirely. If we make it more generally known that radium and the roentgen rays will prevent these growing scars and generally cause their disappearance, patients will be more liable to seek assistance. While keloids or hypertrophied scars occur more frequently in the colored race, they are by no means confined to the colored race, and most patients who have come to me for treatment of this condition have been white. The underlying constitutional cause of the formation of keloids I believe is not known, but the exciting causes are known to all the members of this section, and since the exciting cause cannot be prevented, we need give it no consideration; we shall deal only with the neglect of actual keloids. Usually the patient seeks relief because of deformity or for cosmetic reasons, but occasionally pain is a prominent symptom and brings the patient for treatment. In other cases the keloid may cause actual mechanical obstruction, as when they occur on the feet and interfere with the wearing of shoes.

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The roentgen rays have long been used in the treatment of keloids, not only by myself but by many others. MacKee has been especially prominent in calling attention to the value of this method of treatment. The early work was done, as most radiotherapy was done early, by fractional and indefinite doses. Even with this indefinite technic some brilliant results have been obtained. Even today with more definite technic, much skill and much keen judgment will be necessary to obtain the best results, for no two cases react in exactly the same way. Generally, the aim should be to produce a progressive atrophy without erythema or destructive effect on the skin or overlying epithelium. The technic will vary considerably with the size or thickness of the keloid, especially in the cases in which the roentgen rays alone are used. The thicker and older keloids will require more filtration and correspond-

Fig. 1.—Appearance of patient Oct. 6, 1919, with a keloid following operation for an enlarged gland. He was given one full dose of roentgen rays Oct. 6, 1919, and excised within a few days. He was treated again with the roentgen rays Oct. 23, 1919; Nov. 29, 1919; Dec. 20, 1919; Jan. 17, 1920, and March 13, 1920. The second photograph was taken Jan. 17, 1920.

ingly longer treatment. In recent cases of hypertrophied scars, in which the scar tissue is still quite young, considerably less treatment and less filtration is necessary. In these mild types one can use to advantage 5 milliamperes of current, 2 millimeters of filter, with a focal distance of 8 inches, a parallel spark of 9 inches, for a period of two minutes. This will give approximately $\frac{8}{10}$ of an erythema dose, and will be within safety limits. This treatment can be repeated in three or four weeks. It must be borne in mind that the factors given will vary in value considerably according to the instrument used, and

one must familiarize himself with the value of each particular instrument. In the thicker and older cases of keloid which one is trying to eliminate by the roentgen-ray treatment alone, it is desirable, when possible, to obtain a cross-firing effect. When this is possible, the area to be affected is divided into two or more portals of entry, and the rays so directed through these various fields that the deeper portions of the rays will cross in the deepest portion of the tumor. In these cases it is desirable to use the following technic: 5 milliamperes with 6 millimeters of filter, a focal distance of 8 inches, and a parallel spark of 9 inches for a period of eight minutes.

TREATMENT BY RADIUM

Radium will give very similar results if used in corresponding doses; that is, in the treatment of keloids one can produce results almost identical with those obtained from the use of the roentgen rays. Plaques or capsules may be used. One should learn the value of the

Fig. 2.—Appearance of a patient June 24, 1919, with a keloid following the pinching of a small papule. It had been burned out with acid but recurred. One dose of roentgen rays was applied June 24, 1919. The keloid was immediately excised and treated July 23, 1919, with 50 mg. of radium in 0.5 mm. of silver, and 2 mm. of rubber, applied one-half hour. Aug. 18, 1919, 100 mg. of radium were applied for one hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. Sept. 29, 1919, 100 mg. of radium were applied for thirty-five minutes, filtered through a 0.5 mm. of silver, and 1 mm. of rubber. Nov. 11, 1919, 100 mg. of radium were applied for half an hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. The second photograph shows his appearance March 22, 1920.

particular specimen that is being used, and it should be used long enough to produce an erythema dose, with a filtration equal to approximately 0.5 mm. of silver. This will eliminate about 98 per cent. of the beta rays. The duration of treatment will vary according to the size of the specimen used and the size of the keloid which is to be treated. In order to use the radium skilfully, the value of the speci-

men over a given area with the filtration above mentioned at a given distance should be known. From this the necessary distance and area can be calculated according to well-known methods. A 50 mg. capsule in 0.5 mm. of silver and 1 mm. of rubber in direct contact will produce an erythema dose in one hour.

SURGERY COMBINED WITH RADIOTHERAPY

My chief object is to emphasize the value of this combination. It is not new, and is only original in the sense that I have arrived at the conclusion of the value of this treatment, and have been recommending it for a number of years independent of the knowledge that others have been doing likewise. MacKee¹ says in very large keloids it is preferable to ablate, and then apply the roentgen rays as prophylactic. This may be done also in small keloids in order to obtain a perfect cosmetic result. He also says:

I have never observed a recurrence after roentgen-ray treatment. When one is treating a very large keloid so much radiation is necessary that there is danger of a degeneration or ulceration with secondary carcinoma formation. At any rate, in the very large keloids one often will fail to reduce them absolutely flat with the skin. Therefore, for cosmetic reasons alone it is advisable to excise and then treat.

The method that I have been recommending as a rather routine procedure is the application of the roentgen rays to the keloid area preceding the operation, preferably a few days to two weeks before, and of a dose such as one would give if the rays were to be depended on to remove the keloid. The keloid, or hypertrophied scar, is then carefully excised. This can be done best when there is sufficient loose tissue or skin round about to close the wound without too much stretching, and I believe that the surgeon should excise as nearly as possible to the outline of the keloid and not attempt to excise wide of the area. I have had surgeons unfortunately make a wide incision such as they would make when removing a malignant growth. This extensive excision only increases the area of scar tissue, for even though the keloid is excised, there will always be a scar. The advantage of excision and combined anteoperative and postoperative roentgenotherapy or radiotherapy consists in the reduction of the scar to the level of the skin, and in many instances of a decrease in the total area of the scar. I usually advise a full dose of roentgen rays within a week or ten days after the excision of the scar. The patient is then seen weekly, and if there is any tendency toward recurrence, more treatment must be given. Three or four applications of the rays should be given to guard

1. The Roentgen-Ray Treatment of Skin Diseases. J. A. M. A. **65**:1886 (Nov. 27) 1915.

Fig. 3.—Appearance of patient Jan. 21, 1913, who developed a keloid following a burn when a child. Fourteen fractional doses of roentgen-ray treatment were given between Jan. 21, 1913, and Dec. 22, 1913, each application measuring about half of a skin dose. The second photograph shows her appearance Sept. 9, 1916. The scar is soft and healthy.

Fig. 4.—Keloid following sunburn; it was treated with the roentgen ray, excised and again given roentgen-ray treatment.

Fig. 5.—Keloid following a burn; treated with nine fractional doses of roentgen rays.

more certainly against a recurrence of the keloid. In several of my cases there has been a tendency toward recurrence following this excision, but in every instance it was thoroughly controlled by either the roentgen rays or radium. In some instances, in which there was localized thickening in the scar, I seemed to get more benefit from the local application of the radium, and this effect seemed to be slightly more positive than when I depended on the roentgen rays.

CONCLUSIONS

1. Keloids should be treated by radiotherapy as early as the hypertrophy of the scar can be recognized.
2. Radiotherapy can be depended on — either the roentgen rays or radium — for the reduction of a keloid.
3. The best results will generally be obtained when radiotherapy is combined with excision. If applied before and thoroughly after excision, a flat, soft, smooth and inconspicuous scar should be found.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WILLIAMS, SMITH AND PFAHLER

DR. NORMAN WALKER, Edinburgh, Scotland: Malignant diseases of the skin have a practical importance in connection with certain industrial processes in our country. The Home Office recently requested that I investigate the distribution of malignant growths in the skin in connection with shale workers. I used to see a bad case occasionally in my time, but I had no idea that the condition was so widespread as it turned out to be. The shale industry gives employment to several thousand men and I had an opportunity of inspecting many of them. Much light may be thrown on the possible cause of these cancers by the investigation of industries. It did not take much investigation to find that we go far too wide when we talk of tar, pitch and paraffin as the causes of these growths. It is possible to pick out the particular kind of work that produces them. The men know this very well. The "green sheds" are the ones that produce these disorders, and wise men refuse to work there, for a large percentage of men working there are afflicted. Men who have worked for twenty-five years may show no irritation. It takes from three to five years to show any irritation, and usually it is seven or eight years before malignancy develops. These growths are of the type of senile keratoses and the patients, as a rule, do not see the doctor about them. They have learned that the application of crude hydrochloric acid is sufficient to cure them. The men who have worked in shale for a number of years are scarred all over with the lesions they have removed. In some instances the growths spread to the glands and kill the patient. The interesting point is that in this particular industry the lesions are limited to the arms and legs, which are exposed. All sorts of precautions are resorted to by the men. If they smear their arms with castor oil before going in, the risk of irritation is greatly decreased. I also inspected the briquet industry in Cardiff, where they mix coal dust with pitch. A great many of the workers had growths, but they were not at all like the paraffin growths. They were found occasionally on the hands and on the scrotum. The most remarkable finding was their presence on the neck. Further, most of them presented

a remarkable sensitiveness to light. One man told me that he felt so much agony on a sunny day that on sunny holidays he retired to his coal cellar where it was perfectly dark, in order to get relief from the pain. About three months ago a man walked into my clinic with a malignant tumor on his hand and other keratotic lesions. He was employed in mending fishing nets. There were only four lesions and two had cancers caused from the tar which was used on the material in the nets. There are three types, the tar, the pitch and the oil cases. These cases are evidently due to certain peculiarities in the skin of the person. About 25 per cent. of the men in the green sheds were affected, a much smaller percentage of the pitch workers and a much larger percentage of the tar workers. A Belgian doctor told me that in the Brussels briquet works during the war there was a great deal of carcinoma, affecting 50 per cent. of the workers. These cases are very much like some of the roentgen-ray cancers and the cancers that sailors and other outdoor workers have. Epithelioma of the lower lip is practically never dealt with by dermatologists in our country. We send these cases to the surgeon. Everyone is agreed as to the importance of early diagnosis.

Hebra is reported to have had four cases of lupus carcinoma. I have had four in my wards at one time. In the early years of roentgen-ray treatment, we had cases of lupus from all over the country. Like everybody else, we did not know its dangers and gave doses which would be regarded as criminal now and the number of those patients who have developed carcinoma since that time is appalling. I think I have had between fifty and sixty cases of lupus carcinoma from this cause. If the patients could all be kept under observation one would not need to worry. I have operated at least twenty times in one case for the removal of carcinoma. But when one gets people of moderate intelligence, who know the dangers, and after having had one roentgen-ray cancer removed come up a few years later with a growth the size of a walnut, it makes me consider very seriously whether we ought to advise roentgen rays in the treatment of lupus. Where it has developed, the dermatologist can manage it better than the surgeon. The prognosis is bad enough, but all patients I have seen and operated on have lived some years, and some of them many years.

As to keloid, I have always been of the impression that excision is the worst possible treatment, but I have not tried excision in connection with roentgen-ray treatment. I have come to regard radium as the proper thing for these cases. Where it was not available I have had excellent results from carbon dioxid snow.

DR. WILLIAM CARPENTER MACCARTY, Rochester, Minn.: Many men working on epithelioma lay more stress on tobacco as an etiologic factor. My associate, Dr. Broders, recently published a very interesting study of epithelioma, in which he adheres to the probability that tobacco plays a rôle. Very little is ever said about the effect of sunburn. Having studied the skin of a few thousand farmers in the Northwest, who are exposed to the sun, and after studying epithelioma in many of them, I believe that sunburn plays an enormous part in the development of these growths, perhaps even a greater rôle than does tobacco. The lips of the farmers are always sunburned in the location in which epithelioma is most common. In my experience, epithelioma arises usually from the outer portion of the lip and not inside next the gum. Almost daily, in our clinic, patients, their relatives, nurses and physicians come in to inquire whether or not to have a mole removed, and I advise against this procedure unless the mole presents some

definite change or is in a location subject to frequent injury. Speaking of epithelioma as types, Dr. Broders has shown that a single epithelioma may contain prickle cells, a glandular arrangement of the cells, and often a squamous epithelioma, frequently in the same section, so I do not believe that a basal cell epithelioma is as much of a type as we have thought. In connection with carcinoma of the stomach I found that the patients who had been operated on and had an advanced degree of differentiation of cells lived much longer than the patients with no differentiation. An epithelial pearl is the result of a high degree of differentiation.

Dr. Smith's contributions to the subject of neoplasia are, perhaps, the most valuable that have ever been made. I believe, firmly, that the secret of cancer will be found by a biologist and not by a pathologist.

DR. JOHN E. LANE, New Haven, Conn.: It was intimated that we might abandon surgical procedures for cancer of the lower lip in cases in which metastasis has begun, the question being asked whether radiotherapy might not be as effective as ablation. While there has been great improvement in the technic of radiotherapy recently and in the results of it in carcinoma, it seems to me that in the present state of our knowledge we must answer that question with an emphatic "No." For the present the best procedure appears to be ablation followed by radiotherapy. Radiotherapy should not be neglected in inoperable cases, as there is frequently a good chance of arresting the progress of the disease for a time and an occasional unexpected cure is made. Dr. Williams' position as to the removal of moles is sane and conservative. In case of the deeply pigmented moles, however, it would seem wise to excise them or destroy them with the cautery whenever possible. It is frequently too late to save the patient's life after such moles begin to show signs of activity. I can see no point to Dr. MacCarty's advice to patients not to have moles removed. If moles are an annoyance for any reason, even that of unsightliness, I can see no objection to removing them. It can be done without much scarring and there are practically no ill effects from their removal.

DR. AUGUSTUS RAVOGLI, Cincinnati: The small growths which seem to be entirely insignificant and which last sometimes for one or two years without producing any trouble are often the beginning of an epithelioma, and do not presage anything less than the fight of the cells against the entrance of the periblastic element. When the cancer is present in the epidermis, we have epithelial cells of pathogenic nature making their way into the tissues of the derma. The normal cells put themselves on the defensive to stop the invasion of the heteroplastic cells. This forms a kind of pearl, as we term it. When the cells begin to get down into the corium and the derma, the collagenous textures try to involve these cells, and they form the alveoli, which contain some of the large epithelial cells which constitute the exact features of the cancer of the skin. It is merely an effort of the living organism to stop the progress of these cells. I have seen this epithelial infiltration go deep into the ducts of the sweat glands and invade the coil glands and from there invade the other tissues of the deep corium. The epithelioma following the roentgen-ray burn is the result of a parasitic infection. A few years ago I exhibited a case of cancer en cuirasse. The growth extended over the whole breast. It was the consequence of a burn from roentgen rays.

As to the keratoses and precancerous conditions, I do not see any difference between them, except that the cells are limited to the epidermis. When these cells have a chance to invade the corium, cancer follows. The bite of an insect or any irritation in the vegetable world is capable of causing tumor, just as in the animal tissues.

DR. WILLIAM H. GUY, Pittsburgh: The results reported, excellent though they are, should not be contrasted with statistics that surgeons furnish. The greater number of men who are doing this work have come to the conclusion that any one may obtain as good or better results with radium and roentgen rays than with surgery, regardless of whether or not neighboring metastases have occurred. Because of poor surgical results, most careful surgeons refer these cases for radiotherapy alone or combined with surgery either as a pre-operative or a postoperative procedure. Some of the previous speakers have mentioned the bad results from roentgen rays, in contradistinction to those obtained with radium. In the smaller type of growth these bad results can be obviated by screening with lead up to the margin of the growth, so that the roentgen ray does not fall on any but diseased tissue. I believe that as good or better results can be obtained with radium, because a smaller dose can be applied and because we are shooting with a rifle instead of with a shotgun, and the radiation from the gamma ray will reach to the greatest possible extent the depth of the lesion. I understood Dr. Pfahler to say that he recommends excision only in the larger growths, and I agree with him. In the not too extensive case one may obtain just as good results without excision, except that a considerable amount of time may be necessary to obtain that result.

DR. J. M. KING, Nashville, Tenn.: I have seen a few cases of carcinoma of the face completely relieved by extirpation of the glands, followed by roentgen-ray treatment. I have removed some keloids and followed the excision with the roentgen rays, with very good results. I have treated some keloids on the face one inch thick with a screened Coolidge tube and have obtained excellent results. Extirpation would probably have resulted in worse scarring than from the roentgen ray alone. I had a patient who when 19 years of age was stung by a wasp on a mole just below his left eye. This soon developed into a carcinoma. When he was about 21, the growth was about the size of a quarter of a dollar. The acid from this sting might have been the etiologic factor in this case. Many more carcinomas are found in the stomach and about the cervix uteri than in any other part of the body. Perhaps some acid substance excites the production of the cancerous cell.

DR. RICHARD L. SUTTON, Kansas City, Mo.: About eight years ago, Dr. Lain first spoke to me about his method of clinical classification, a plan which has recently been worked out pathologically, and in a most admirable manner, by Broders. At that time, I had always been firmly of the belief that all cases of squamous cell carcinoma of the lip should go to the surgeon first, and afterward to the radiotherapist. Dr. Lain succeeded in convincing me, however, that many of these cases, especially if taken early, can be cured by radium and the roentgen ray. Hazen and Bloodgood have shown that the majority of carcinomas in this region are of the prickle or squamous cell type. Seborrheic keratoses should be divided into three distinct groups: (1) keratoses of the nevoid type, (2) keratoses of the verrucose type, and (3) keratoses of the keratoid type. The last named is the most dangerous of the three. This is the type to which Dr. Hazen ascribes the high percentage of malignancy. The point brought out by Dr. McCarty is important. In my opinion, tobacco

plays an important part in the causation of these lesions. Frost bite also is a prominent predisposing factor in some instances. With regard to the treatment of keloid, Dr. Pfahler's suggestion is a good one, and I shall give it a trial. In combating the smaller lesions, carbon dioxid snow is a valuable agent, as Pusey, Norman Walker and others have shown.

DR. HAROLD N. COLE, Cleveland: Tobacco has been largely responsible for carcinomas around the mouth. These growths rarely occur in women. Perhaps in the next generation we shall see more since so many women now smoke.

DR. WILLIAM C. MACCARTY, Rochester, Minn.: I did not intend to say that tobacco has nothing to do with the production of epithelioma, but that I believed that sunburn was also an important factor, and that when we know the truth we may find out that it is more important than tobacco. I dare say that 75 per cent. of the people in this room use tobacco in some form, but probably none of us has an epithelioma of the lip.

DR. HOWARD MORROW, San Francisco: We might divide these carcinomas of the lower lip into the deeply infiltrated and those without much infiltration. I do not think it matters whether the superficial ones are treated with radium, roentgen rays or proper excision. Superficial carcinomas should not be treated by any other methods than those mentioned. Treatment with liquid air and other caustics is still mentioned in many textbooks, but we should not adopt this form of treatment, because it is dangerous. I have had many cases of keloid treated by excision and subsequently by radium therapy and the results have been most gratifying.

DR. GEORGE E. PFAHLER, Philadelphia: I have succeeded in curing practically every one of 100 patients with epithelioma of the lip who did not have any metastases in the glands, and who had not been treated previously by caustics or surgical incision. No other treatment can equal that result. The treatment has been, as a rule, the local electrocoagulation of all areas of the disease, including about one-eighth inch around the growth, by means of the high frequency current. I then treat the lip area and the glandular area, usually with the roentgen rays. The same result can be accomplished with radium if you have enough of it, and in none of these cases have metastases developed in the glands. The diagnosis could not be questioned.

When metastases were present in the glands, I have asked the surgeon to excise them and then I treat the whole area thoroughly with deep roentgen-ray therapy. Recently I began to treat a few patients by the introduction of radium needles into these metastatic tumors. I would like to see Dr. Smith carry on the study of irritation. I believe we would learn a great deal about the histology and development of these tumors, and about the effects of radium.

DR. EVERETT S. LAIN, Oklahoma City: I was pleased to know that the etiologic factors as recorded from larger numbers of patients closely correspond to my own findings. Most of the lower lip cancer patients are those who are out in the open air and are subjected to sunburn. Most frequently they are thin skinned blonds. I am certain that sunlight is a predisposing factor in a large number of the cases as well as the use of tobacco. My technic was very uncertain in the early years. In recent years I have most frequently begun by using the beta and gamma rays for the first and perhaps second series of treatments. Later I use only the hard or gamma rays whether or not there is deep glandular involvement. A similar routine has been practiced in the use of roentgen rays. I have been giving one or more series of crossfire, deep roentgen-ray treatments in all cases of suspected glandular

involvement, screening with 3 or 4 mm. of aluminum. Only five of my patients were women and two of these were smokers.

DR. CHARLES M. WILLIAMS, New York: Classifying lip cancers into those that are readily cured and those that are more malignant will be a great help in selecting the proper treatment. Kangri cancer is believed to be caused by heat, although Ross is of the opinion that the soot and smoke are the important causative factors.

DR. EARL D. CRUTCHFIELD, Galveston, Tex.: There is a distinct basal cell type of cancer which may clinically be considered a nonmalignant growth. The differentiation of prickle cell carcinoma and basal cell carcinoma is simply one of definition. I have seen two cases, both of the basal cell type, and the gland metastases were of the squamous cell type. Pearls are not more malignant, but in many of the rapidly growing types and the rapidly infiltrating types there is a tendency toward degeneration of the epithelium. On the other hand, many of these tumors show no pearl formation. I think the stage in which the cells divide has much to do with classification.

DR. ERWIN F. SMITH, Washington, D. C.: All I have wished to do all these years was to get the oncologists to see things in a new light and not depend chiefly on section cutting, not that I deprecate that, but that I conceive something more and different to be necessary. If I can wake them up to that, I think I have done my share of work even if I do not make any animal experimentation. Already cancer specialists have begun to study crown gall from their own standpoint, not only in the United States, but also in England, Germany and other countries, and C. O. Jensen of Copenhagen, is on record as saying: "I fully share the opinion of Erwin F. Smith that crown gall is a new formation which (irrespective of its cause) can be placed side by side with the real malignant tumor formation in the higher animals."