

If drugs are advised, the best preparations, the best method of administration, and the beginning doses are carefully pointed out. It is also emphasized that if a dangerous condition can perhaps be overcome by a strong drug used fearlessly but thoughtfully, it should be used, as a surgeon uses his knife, to save, if possible, a desperate case. The management of convalescence and of incurable diseases is carefully mapped out.

Throughout this senior year two clinical lectures a week are given at which the symptoms and signs of disease are carefully noted and written down, and the most rational possible treatment then given. The patient, on his return to the clinic a week later, is particularly questioned as to each detail of his previous history, and the results of the treatment are written down opposite the treatment given on his previous visit. This graphically shows the mistakes in diagnosis, mistakes in judgment, in the choice of drugs, dose, or management, as well as the success of treatment. Also, reference to the probable prognosis written down at the first visit shows how much was expected of the treatment. The senior students all through this year act as clinical assistants in the dispensary, taking histories and writing prescriptions under dictation.

At the end of this year, after passing a written examination on therapeutics, it would seem that the graduate should know something of this subject.

All this instruction should be under the management of the professor of materia medica and therapeutics, and thus all can be amalgamated into one progressive homogeneous course.

That this ability to practice the art of therapeutics as we understand it need not be lost after graduation, hospitals should more especially individualize their medical cases and should avoid the use of cut-and-dried formulas as much as possible.

Hospitals are preventing the establishment of the metric system almost as fast as the medical schools are inaugurating it. They should use the easy decimal system; translations from one system to the other are hopeless.

Postgraduate schools are more and more meeting the demand of their students that more time be spent on therapeutics, and hence we need not urge them to emphasize this branch of medical need.

Lastly, the therapeutic societies have come to stay, and the greater the number established the more rapid the advance in this neglected science. It is absurd for societies and sections devoted to the practice of medicine to declare that therapeutics is a branch and part of medicine. No one denies it, but for the last twenty years it has been a neglected part, and it should now be given special study and special discussion. Where would the practical societies stand without the work of the pathologists? On the other hand, how helpless would the trained diagnostician be, how would the patient fare, without the work of the pharmacologist and the study of rational therapy? Societies devoted to the study of therapeutics will do much to prevent the phrase "how do you treat pneumonia?" and abolish the ridiculous, often absurd, often dangerous advice given in the medieval formulary departments of our medical journals. Some of the worst errors in prescriptions are copied from journal to journal because some man of renown was supposed to have some time recommended that particular prescription, though he may not be guilty of the mistakes in it.

Original Articles

THE THERAPEUTIC USE OF X-RAYS.

THREE YEARS AFTER.*

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CHICAGO.

In March, 1900,¹ in November, 1900,² and in February, 1902,³ I read papers before this society on the therapeutic use of *x*-rays. The first paper was a consideration of their use in skin diseases; the second, a report and a demonstration of lupus successfully treated with *x*-rays; the third, a report and a demonstration of a number of cases of various kinds showing the results of exposures to *x*-rays. The cases reported included lupus, epithelioma, senile keratosis, recurrent carcinoma of the breast, deep-seated carcinoma of the head and neck, sarcoma, keloid, pseudoleukemia and leukemia. In another report⁴ the use of this agent in various forms of dermatoses was considered. Three years now have passed since the last of these reports, and I venture to hope that it will not be unprofitable nor without interest to review the subject and to undertake to estimate from the results the therapeutic limitations and possibilities of this agent. I fear this paper will appear unduly personal, since I am only undertaking to review my own experience, but for this I offer the apology that one's personal experience is that which he can best review. I hope it will not seem that I am overlooking the work of the many men who have made valuable contributions to the subjects on which I am giving my own experience.

So far as the use of *x*-rays in cutaneous diseases is concerned, that can be quickly summarized, for there is pretty general unanimity in the experience of dermatologists.

HYPERTRICHOSIS.

The use of the *x*-rays for the permanent removal of hair has not equaled my early expectations. In my experience I should say that they have given satisfactory results in about 50 per cent. of the cases treated, but to get these results has required long and painstaking treatment, and in some cases even this has failed. This application is so beset with difficulties that I do not undertake it unless the conditions are very urgent. Hypertrichosis is the one condition in which my experience with *x*-rays has been less satisfactory than I anticipated.

SYCOSIS AND TINEA.

In sycosis and tinea sycosis the results with *x*-rays are exceedingly satisfactory and in some intractable cases they give results that are obtainable by no other method. The results are permanent. Some of my cases have been well more than three years.

ACNE.

In my experience acne offers one of the best illustrations of the value of *x*-rays. It is little short of marvelous to see the improvement produced in most obstinate acnes from careful *x*-ray exposures. I have treated a large number of acnes by *x*-rays, and the results in most cases have been good. I have occasionally had results that were not completely successful, even after long-

* Read before Chicago Medical Society.

1. Journal of Cut. and Genito-Urinary Dis., July, 1900.

2. THE JOURNAL A. M. A., Dec. 8, 1900.

3. Ibid., April 12, 1902.

4. American Dermatological Association, May 31, 1901.

continued treatment, these partial failures being attributable, I believe, to failure to get enough *x-ray* effect, but I believe I can say that I have never failed to see an improvement take place after a reasonably long period of treatment, and in many cases I have seen results which no other method can approximate.

As to the permanency of the results, the patient may occasionally have the recurrence of a lesion, but in some cases not even this has taken place. When relapses have occurred, they have shown themselves easily amenable to treatment. The results are attributable, I believe, chiefly to the decrease in the activity and size of the sebaceous glands produced by the *x-rays*. In these cases of acne, the gaping follicles decrease in size, comedones disappear, oiliness is diminished, and the appearance and texture of the skin are greatly improved. In many cases the improvement is quite remarkable.

Of course, the application of *x-rays* for acne has to be carried out with great care, and it should not be undertaken until the operator knows with reasonable assurance the *x-ray* effect he is going to produce by his exposures. The objection to this method is that, if one proceeds safely, the treatment extends over a considerable period of time, perhaps several months. Unfavorable after-effects on the skin, which have been urged as a possible danger here, I have not seen, and I believe the treatment can be carried out without any danger, immediate or remote.

The favorable results in acne I have seen in all types of the disease: in simple juvenile acnes in healthy subjects and in the most deep-seated indurated acnes in patients who are out of health. Of course, the method has its greatest usefulness in the deep-seated, severe and otherwise intractable cases of acne indurata.

ROSACEA.

In rosacea the results have been quite as satisfactory as in acne. Not only can the folliculitis be controlled, but in some of my cases I have been surprised to see the nose become of normal color and contour again; and, what was more surprising, dilated blood vessels disappear. These cases show only a very slight tendency to relapse; in some cases that I have had under long observation and treatment the results have been permanent. I had one case of as ugly rosacea as one often meets, which has been practically well for three years, and without any treatment has not had a relapse in the last two years.

HYPERIDROSIS.

From the effect of *x-rays* on the appendages of the skin I suggested⁴ the theoretical possibility of the value of *x-rays* in the treatment of excessive localized sweating. The value of the agent in this connection has been confirmed by the experience of several operators.

INFLAMMATORY DERMATOSES.

The use of *x-rays* in chronic inflammatory dermatoses has proved of much value. In chronic indurated eczema, my experience, like that of numerous others, testifies to their value. They have been particularly useful in the chronic intractable eczemas of the hands. I have also had satisfactory results from their use in chronic indurated eczema of other parts and in acute exacerbations of old eczemas. Their effect in relieving itching in these cases is frequently quite marked, but sometimes fails. Their effect is not limited to the relief of itching, but there is a positive influence on the met-

abolism of the affected tissues that frequently causes the complete disappearance of the disease. I have also seen the rays fail to produce any appreciable effect on some cases of eczema. I have in mind particularly two cases of that distressing form of eczema of the face, which we call neurotic, that is seen occasionally in people beyond middle life. The only two cases of this sort that I have had the opportunity of treating thoroughly with *x-rays* have proved totally rebellious to them, as they have to everything else.

In the subacute or chronic inflammatory diseases of the skin, accompanied by a good deal of scaling, such as psoriasis and lichen planus, the effect of the rays is very beneficial. Their application is free from the disagreeable circumstances of the usual local treatment of these conditions, and in some cases they do more than can be done by other means. But here their value is not unique, for we have other satisfactory methods of treating these conditions.

LUPUS ERYTHEMATOSUS.

The results in lupus erythematosus do not show that *x-rays* furnish the much-needed effective method of treating that extremely uncertain affection. Decided improvement may take place from their use, but one can offer no assurance of a satisfactory result. They are inferior, in my experience, to the application of the high-frequency current.

PRURITUS.

In pruritus ani and vulvæ I have seen the benefit from the use of *x-rays* that other observers have reported. The temporary relief of itching has been very common in my experience, but I am not sure that any case has been permanently cured. The relief that can be given to these miserable sufferers, however, fully warrants the use of the treatment. In the indurated dermatitis that frequently accompanies these cases, I have seen the same improvement as in eczemas of similar type elsewhere.

PIGMENTED AND VASCULAR NEVI.

In both pigmented and flat vascular nevi my experience with a few cases has led me to believe that *x-rays* offer a method of treatment of distinct value. The most satisfactory result in pigmented nevi has been in the case of the daughter of a physician who had a hairy, pigmented nevus, involving the entire right side of the forehead and temple from the eyebrow to the scalp. The skin was black, had a thick, horny layer, and was covered with a growth of black hair, quite as heavy as that on the scalp, with which it was continuous. By careful treatment all the hair was removed and the skin of the surface made almost normal in appearance. It is slightly darker than the adjacent skin, but is smooth and soft and of good color. We succeeded in this case in getting an eyebrow and a hairy border of the scalp of normal contour, so that practically the deformity was entirely obliterated. This patient has now been well for two and one-half years. I am sure that such a result could not have been obtained by any other method. In a few other cases I have been able almost to obliterate similar but smaller nevi.

In the only two vascular nevi I have treated I have been able to cause improvement which was satisfactory to the patients. In neither of these cases has the red color been entirely removed, but it has been converted from a dark conspicuous red to a light, pinkish color that is very much less obtrusive; and in doing this the texture of the skin has been improved, so that the skin

over the surface of the nevus is smooth and soft. There can be no doubt of the positive improvement in these cases, because small outlying areas that were left as checks to determine accurately any change of color remained much darker. I do not mean to suggest *x*-rays as a method entirely satisfactory in these cases, but until some more satisfactory method of treating them is devised than we now have I believe this method has here a field of usefulness.

KELOID AND SCARS.

In my demonstration three years ago I showed a case in which a large keloid on the arm had been made to disappear under *x*-ray treatment. There had been no recurrence of this keloid two years after, when I last saw the patient. I have treated successfully several typical keloids, most of them on the chests of women. The keloids flattened down into soft, pliable, white scars, and the pain which exists in some of them completely disappears. Such cases seem to leave no room for doubt that keloid can be cured by this method—which, I believe, is more than can be said for any other. *X*-rays also offer an eligible method of treatment of other handlike scars.

LUPUS VULGARIS.

There is unanimity of opinion among dermatologists as to the value of *x*-rays in lupus vulgaris, and my experience corroborates this. I have seen but one case of lupus vulgaris which failed to yield satisfactorily to the rays, and that was a case of lupus of the face extending deep into the tissues, which had recurred after a plastic operation. In my experience, lupus has yielded readily to *x*-rays, and when the treatment could be carried out satisfactorily the results have been all that could be hoped for. As to the permanency of the results, the patients whom I showed symptomatically cured at the meeting of this society four years and three years ago have had no recurrences. I have had some failures in lupus vulgaris, but they were failures which, I believe, may be reasonably attributed to the fact that it was impossible, on account of the patients, to carry out the treatments satisfactorily.

There is surely no other method of treating lupus vulgaris that stands in the same class with *x*-rays, except Finsen's method. The results from Finsen's method are as good, but I believe, even in my limited experience with lupus vulgaris, that I can duplicate any of the results of Finsen's method. *X*-rays have certain very decided advantages over Finsen's method. The results are more rapidly obtained; the treatment is applicable to mucous membranes; it will reach lesions much more deeply situated; it does not require the aid of supplementary painful, mechanical or caustic methods of treatment; there is no discomfort from the application of pressure to the surface to drive out blood; and the treatment can be applied at one sitting to large areas, while in Finsen's method it is impossible to treat more than about one square centimeter of diseased tissue at one time. I have treated some cases of widely disseminated and very extensive lupus in which treatment by Finsen's method would have been unending.

TUBERCULAR GLANDS.

I have had a somewhat extensive experience in the treatment of tubercular glands, especially those in the neck. My experience has been variable. In the treatment of primary cervical adenitis without involvement of the skin, in many cases I have been able to reduce the size of the glands and by long-continued treatment

to cause them to decrease to the point of disappearance. In other cases, however, there has not been much improvement. In the treatment of cervical adenitis, in which there was already involvement of the skin, my results have been more positive. In nearly all cases it has been possible to cause healing of the sinuses and distinct improvement in the condition. A case referred to me three years ago by Dr. A. J. Ochsner, which is about the most severe of this sort that I have treated, illustrates the extent of the results that can be obtained. This patient had had repeated operations, extending over several years, for tubercular glands on both sides of the neck and in both axillæ. Operation after operation had been done until all the tissue that could be spared had been taken out. The disease, however, had recurred in all four localities. There were numerous sinuses and the skin and the subcutaneous tissue were thickened and indurated and unhealthy. Under *x*-ray treatment given twice a week for three months the sinuses all healed, the tissues became healthy, and she has remained well now for three years, practically without further treatment.

TUBERCULAR JOINTS.

My experience in tubercular joints has not been extensive. In some cases the rays have not appreciably affected the condition. In a few cases, however, there seems to be little doubt of very positive benefit. I have treated a very severe case of this sort during the last year for Dr. J. B. Murphy. In this patient, a young man, there were tubercular lesions of many joints—the feet, the ankles, the knees, the wrists—some of them with involvement of the skin, some of them without. Under *x*-ray exposures nearly all the discharging lesions have healed, the patient has become so that he can use his joints without pain, the swelling has very greatly decreased and he has gained forty pounds in weight. From being an invalid on crutches and almost completely confined to bed he has got on his feet again, is able to exercise without discomfort, and has been able to go to New Mexico alone to spend the winter. How much of this is due to *x*-rays may be open to question, but it is certain that during the time that he was subjected to the exposures his condition vastly improved without change in his surroundings or in his other treatment.

ABDOMINAL TUBERCULOSIS.

In one case of abdominal tuberculosis, which I have treated during the last two years in conjunction with a surgeon of Chicago, there has been improvement, which has been attributed by the surgeon very largely to *x*-rays. In his opinion, I believe, it rendered possible an operation for the relief of an intestinal obstruction, which has been followed by great improvement of the patient. I have no other cases of this sort that have had extended treatment, but on theoretical grounds and from my small experience I believe the method is worthy of careful trial, not; however, at the expense of omitting other means for combating the condition.

DEEP SINUS.

I have treated numerous deep sinuses of various sorts with *x*-rays, usually without radical relief. In one abdominal sinus, however, the result was surprising. This was in a young woman, in whom a laparotomy had been done for pelvic abscess. A sinus resulted which resisted all attempts at relief. When she came under treatment she had a sinus between the umbilicus and the pubis, from which there was a very

abundant discharge of foul pus. She was weak and greatly emaciated. Under *x*-ray exposures, extending over a period of four months, there was a rapid diminution in the discharge until it entirely disappeared, and a month after stopping treatment, in June, 1903, the sinus permanently healed. The patient, a woman of large frame, gained fifty pounds in the next few months.

BLASTOMYCOSIS.

In blastomycosis my experience with *x*-rays, extending over a half-dozen cases, has been uniformly favorable. The results have been radical in all except one case, in which the patient would not continue treatment. In all of the cases *x*-ray treatment has been combined with potassium iodid in from 10 to 20 grain doses, *t. i. d.*, and my experience leads me to agree with others that the use of *x*-rays in combination with potassium iodid offers an ideal method of treating cutaneous blastomycosis. In addition to the treatment of demonstrated cases of blastomycosis I have treated successfully by this method two large suppurating, papillomatous tumors, one over the knee, one on the thigh. Both patients were women and both lesions had resisted for at least two years other methods of treatment. The first of these patients, a middle-aged woman, was on crutches and the condition was serious enough to warrant the consideration of amputation of the leg. The use of the leg was entirely regained and there has been no recurrence in two and one-half years.

ACTINOMYCOSIS.

My experience in actinomycosis has been confined to one case in the jaw, in which ulceration had not occurred and the diagnosis was clinical. The patient was referred to me by Dr. A. J. Ochsner. In this case *x*-ray exposures, combined with 20 grains of potassium iodid, *t. i. d.*, was followed by complete and permanent resolution in a few weeks.

I have another case in which the diagnosis lay between actinomycosis and sarcoma, in which the result was remarkable. This patient was referred to me by Dr. L. L. McArthur in September, 1902. Six months previously the patient had noticed a painful tumor in the left side of the breast which at first grew slowly, but then rapidly extended. At the time he was referred to me there was a large tumor occupying the whole front of the chest between the axillary lines and from the lower end of the sternum to the clavicles. It was densely hard, immovable, of purplish color, and involved the skin. Over the center the tumor showed a few small ulcerating points. There were indurated glands in both axillæ. In Dr. McArthur's opinion, it was a case of sarcoma, and the patient had had a piece of tissue excised at the hospital for microscopic examination. After it was too late to get another specimen it was discovered that this was lost, and the diagnosis was never confirmed microscopically. In a little over a month of *x*-ray exposures this mass, which was over a foot in diameter and three inches thick at the center, completely disappeared and with it the axillary glands. He had no other treatment besides *x*-rays. His cachexia disappeared and his health was completely restored so that he was able to return to hard labor. There has been no recurrence, now in over two years. I have seen nothing in the use of *x*-rays more striking than the result in this case.

CUTANEOUS CARCINOMA.

My experience with epitheliomas now covers a large number of cases, including lesions of all descriptions,

from the smallest epitheliomas to larger lesions than I have seen anywhere described, and the results which have been obtained have given me the utmost confidence in the use of the *x*-rays in this condition. I am almost prepared to say that I believe that any cutaneous carcinoma can be cured with *x*-rays. When I say cutaneous carcinoma I mean to exclude metastases or extensions deep into the underlying structures; but this exclusion does not limit the application of this method to cases that are easily amenable to surgical methods, because there are still left certain lesions which from their extent are beyond surgical intervention, and numerous other lesions in which surgical treatment is unsatisfactory or undesirable, if not impossible. As to the class of epitheliomas which are suitable for *x*-ray exposures, I believe it may be said broadly that all epitheliomas are suitable for this method of treatment except those cases in which conservative surgery requires the removal of contiguous glands. For epitheliomas in certain localities the *x*-rays offer particular advantages on account of the favorable character of scars that result. This applies especially to epitheliomas on the nose, of which I have had many cases, to epitheliomas on the ears, of which I have had several cases, and especially to epitheliomas on the eyelids.

I have treated by this method several cases of epithelioma on the lower lid in which there was no involvement of the deeper tissues of the orbit, and in all of these, except one in which the patient would not allow sufficient treatment, a successful result has been obtained without interfering with the function of the lid or in any way affecting the eye. The unsuccessful case shows improvement that has remained permanent for two years. There has not been any relapse in any of the others and one has been well two and a half years.

Among my cases of epithelioma on the nose are a few successful cases of very extensive epitheliomas, involving the tip and the alæ of the nose and the contiguous parts of the cheek, which had failed of relief from operation or in which surgery offered no prospect of relief except by extensive and very mutilating operations. One of these cases is among those I demonstrated three years ago symptomatically cured, and this patient remains well now.

There is a type of epithelioma of the nose which we fortunately see rarely, which is situated deep in the tissues and is of very rapid growth. When patients with this type of lesion come under observation the nose is usually almost completely destroyed. There are large nodular masses at the border which melt away rapidly with great destruction of the tissues. I mention this type of lesion because in two cases of this sort that I have seen, one of which, I thought, had adequate treatment, *x*-rays did not materially check the course of the disease. Likewise, I have failed of successful results in several extensive carcinomas of the orbit. I refer now to the very destructive lesions which we sometimes see that involve the whole orbit and in time leave an enormous cavity. Very great improvement can be made in these cases and the course of the disease can be almost completely checked, but I have not seen radical relief. I have had one very interesting case of this sort in a middle-aged man who had only one eye and had a carcinoma involving that one. The carcinoma had extended from the inner canthus deep into the orbit and involved the contiguous bony structures. This patient has been under my care at intervals for two years. A year ago Dr. Casey Wood, at my sugges-

tion, removed as much of the carcinoma as was possible without destroying the eye, and during the two years I have given him x-ray treatment as vigorously as possible. There has been no superficial ulceration and, in view of the previous history of rapid growth and the course of such cases ordinarily, there seems to be no doubt that in this case we have succeeded in preserving for him a useful eye for two years. How much longer this result may be maintained I do not know, but he is apparently in as good condition now as he was two years ago.

I have failed in two deep, rapidly destructive lesions involving the ear and the surrounding parts. Neither of these patients was well situated for treatment, but I am inclined to believe that I would have failed under any circumstances. These cases about cover the failures which I have had in adequately treated cases of epithelioma without metastasis.

I have had one or two surprising experiences in having epitheliomas get well under very vigorous exposures after I had practically decided that the treatment was a failure. This, I believe, was solely due to unusual resistance of the tissues to the influence of x-rays. I have recently had a case of epithelioma of the forehead of the size of a half dollar, which was referred to me by Dr. Leonard St. John, in which I treated the patient for two months without effect; indeed, the lesion spread under the exposures. The failure was so complete that I went to Dr. St. John and said that I was willing to admit a failure and to have him take the patient for operation. He was generous enough, however, to leave the case to my further care. I then applied x-rays for two weeks, vigorously enough, I am sure, to cause a severe burn in an individual of ordinary susceptibility. The result was that in six weeks I had a smooth, perfectly healthy-looking scar. I think there is no doubt that the explanation of the intractability of this lesion was the unusual tolerance to x-rays of this patient, not of the tissues of the tumor, but of all the patient's tissues, because the healthy surrounding skin reacted only very slightly under severe exposures.

EPITHELIOMA OF THE LOWER LIP.

Epitheliomas of the lower lip, in view of the danger of the involvement of the submaxillary glands, should be attacked by x-rays or by any other method which does not involve removing the contiguous glands, with extreme caution. I have treated 20 cases of epithelioma of the lower lip, most of which were referred to me by surgeons, and in all of which the treatment with x-rays was decided on after operation had been considered. Except one case, these were regarded as favorable cases for x-ray treatment; that is, they were of the superficial type of epitheliomas. Most of them were cases that involved a large surface of the lip but did not extend deeply. In 19 of the 20 cases there was no palpable involvement of the glands. It so happens that 19 of the cases gave healthy scars. Ten of them have been well for more than a year, 9 of them were treated during the last year. One case was that of an old man who had positively declined operation, and who had a large submental and a large submaxillary gland palpable when the treatment began, and that case was a failure.

All of my epitheliomas of the lower lip have been in men. I have treated only three epitheliomas of the upper lip and, curiously enough, two of the three were in women. In two cases I obtained a healthy scar. In

the third, a very old woman with a deep-seated nodular recurrence after operation, there was healing but with a suspicious scar which after a year without treatment, although this was advised, broke down, and at present there is a recurrence.

Unquestionably, x-rays do not offer so radical a method of treating epitheliomas of the lip as does the operation which includes the removal of the submaxillary glands; but, if the removal of these glands is not to be done—and in many cases for various good reasons this is not the practice—all can be done by x-rays that can be done by any other method. I do not want to be understood as advocating the substitution of x-rays for radical operation in epithelioma of the lip, but only as saying that the method is efficacious on the lesions of the lip itself and is entitled to consideration in those cases in which the radical operation is not thought to be necessary or is for any reason impracticable.

As regards the treatment of epitheliomas covering large surfaces, x-rays offer a method of successful treatment for some cases which are so extensive that operation is out of the question. One such case I demonstrated three years ago symptomatically cured, and at the time of this patient's death—from acute illness—18 months later, there was no recurrence except a nodule in the skin the size of half a wheat grain. The possibilities of the method in cases of this sort are shown in a patient, referred to me by Dr. E. M. Marquardt, in which there was a rodent ulcer involving the entire forehead, extending down over the left eyebrow, involving both lids of the left eye, the skin of the nose almost down to the tip, and the upper right eyelid. Under x-ray treatment this promptly got well and, except for a pea-sized recurrence, has remained so for two and a half years. I have at present an old woman who, when treatment was begun, had an epithelioma on the middle of her back larger than a hand and excavated to the depth of an inch at the center. At present this is reduced to an abraded surface the size of three fingers and only slightly depressed. The tissue is free from evidence of carcinoma, but epidermis has not yet formed over the center of the lesion. These are cases in which nothing else offers prospect of relief.

As to the permanency of the results, I presented, three years ago, 7 epitheliomas symptomatically cured with x-rays. Of these 1 patient, who had an epithelioma larger than a hand, died 18 months later from an acute illness, with a recurrence half the size of a wheat grain. The other patients are well to-day. Four of them have had no recurrences, 2 of them have had minute recurrences which were not difficult to get rid of. Two of the cases were simple, small lesions which were not difficult to handle by any method; the other 5 cases were most of them extensive and all of them had failed of relief by previous treatment. In all of these cases, of course, there had been a microscopic diagnosis. My experience as to permanency in my subsequent cases has been quite as good. Where I have obtained a scar satisfactory to myself, recurrences practically have never taken place. Occasionally there have been small recurrences around the border of the lesions, but, as a rule, these have been of no gravity and have been readily handled. I am sure the cases will bear fair comparison as regards permanency of results with any similar number of cases treated by any other method.

One of the early objections to the use of x-rays in the treatment of epitheliomas was the length of time re-

quired for treatment. Occasionally now one finds a patient who is very insensitive to x-rays and in whom it requires numerous exposures to produce the necessary effect; in most cases, however, all the x-ray treatment necessary can be given in a few exposures. I have had numerous cases which have had only from three to five exposures, and in which the entire treatment to the point of production of a healthy scar did not extend over three weeks. A minor objection is that occasionally patients are quite susceptible and a dermatitis occurs which leaves an abraded surface that takes, according to its size, from three to six weeks to heal. I have never, however, seen any of these burns that gave more trouble than moderate tenderness and the slight inconvenience arising from an abrasion of the epidermis. I have never had a sloughing x-ray burn in an epithelioma, although I have thought that I was running the risk of it many times.

SENILE KERATOSES AND LEUCOPLAKIA.

In connection with epithelioma it seems that a word should be said about the treatment of two lesions which are so very frequently the forerunners of epithelioma, senile keratoses and leucoplakia buccalis. I have treated many senile keratoses with x-rays, some of which were not inflamed, and others which had irritated bases and presented the early stage of epithelioma. In some of my cases the lesions have been very numerous over the face, or over the face and hands. Senile keratoses can be made to disappear almost invariably. As there is no other satisfactory method of treating these lesions, and as they are so frequently the precursors of rodent ulcers, a successful method of treating them is no small gain.

I have not been nearly so successful in leucoplakia buccalis. I have succeeded in some cases in clearing off these patches, but I have also failed in some cases.

CARCINOMAS IN THE NECK.

I have treated many metastases of carcinoma in the neck arising from carcinomas in the mouth or on the lip. My experience with x-rays is that they are as futile as every other method in the treatment of the deep carcinomas in the neck. I have had two cases, however, in which there was a development of carcinoma in the scars after operations on the neck for carcinoma, which have been successful. In one of these cases there was a recurrent nodule in the scar on the lip and small nodules in the scars under the chin where glands had been removed; a third operation had been advised by a prominent Chicago surgeon. In the other, a similar case, there was development of small nodules in the scar. Both of these patients have been well now more than two years. In all my other cases the ultimate result has been failure. There has been distinct benefit in some of these cases in the way of relieving pain and of getting rid of much carcinomatous tissue, but in some of the cases there has not been even this.

MIXED TUMORS OF THE PAROTID.

During the last year I have had the opportunity of treating several cases of these curious, and clinically only slightly malignant, so-called mixed tumors of the parotid. All the cases are still under treatment, several of them showing decided diminution in the size of the tumor. In one such case, referred to me by Dr. L. L. McArthur, there has been almost complete disappearance of the tumor which had caused a very pronounced swelling over the parotid and had been gradually growing for several years.

RECURRENT CARCINOMA OF THE BREAST.

I have treated a large number of recurrent carcinomas of the breast, almost every one of which has been referred to me by a surgeon, and all of which were hopeless of other methods of relief. The results have been so surprising occasionally that I have not refused to treat any case unless there was already well-developed evidence of mediastinal or pulmonary involvement or of deep-seated distant metastases. It goes without saying that in such a desperate class of cases I have had failure after failure, and yet in many of the ultimate failures the treatment has been well worth while in healing ulcerations on the chest wall and in similar palliative ways. I am sure also that there can be no doubt that in many of these cases the course of the disease has been greatly checked and the patients' lives have been prolonged in comparative comfort for many months, or even for a year or more.

This statement is notably illustrated in one of the cases which I demonstrated three years ago in which a very extensive recurrence on the chest wall had been gotten rid of between Nov. 1, 1901, and March 1, 1902. This patient had a year of good health and comfort with only a slight recurrence, which yielded to a few x-ray exposures, the only treatment that she had during this time. The disease then recurred again, she declined to return for any further treatment and died after six months. Many similar cases could be cited.

In a good many cases results have been obtained which have proved permanent to the present time. Of the three cases of recurrent carcinoma of the breast which I presented three years ago, one, the patient last referred to, died eighteen months later of carcinoma of the lung; the second case died fifteen months later of carcinoma of the spine without recurrence in the chest wall. The third case remains well to-day. This patient had had two operations and on the third recurrence consulted Dr. Ochsner, who refused to operate further and referred her to me in September, 1901. She then had two ulcers the size of a fifty-cent piece in the scar surrounded by an indurated border of carcinoma. When her case was reported in February, 1902, Dr. Ochsner, in referring to the case, said that in his opinion she would have died before then had she not had x-ray treatment. She has never had another recurrence. She has had several series of x-ray exposures since that time as a precaution, but has now had no treatment for over a year, and she has remained symptomatically cured for three years. She has been in good health during all this time and has been able to earn her living. I have a good many similar cases with symptomatic cures that have persisted for from one to two and a half years.

In April, 1902, a woman, aged 46, was referred to me by Dr. Brannon of Manhattan, Ill. She had had a slowly-growing carcinoma which had been removed in September, 1901, and when she came for x-ray exposures there were nodules along the course of the scar, a large mass of fused glands in the axilla, a similar but smaller mass in the supraclavicular space, and slight edema of the arm. Physically she was much reduced. Under x-ray exposures the recurrence in the scar entirely disappeared, then the supraclavicular glands disappeared, and finally the axillary mass. The edema of the arm disappeared and she was restored to her normal health. She has been symptomatically cured for two and a half years.

On Nov. 19, 1902, Dr. Frank Billings referred to

me a woman, aged 67, with the following note: "Dr. Fenger removed the left breast Nov. 28, 1901. There is, as you will see, infiltration again above the clavicle. There is some dyspnea, but I can find no physical evidence of involvement of the lung or heart. There may be, of course, mediastinal disease now." Under *x*-ray exposures, vigorously given, the puffiness of the supraclavicular space subsided, and the supraclavicular glands, while not disappearing, diminished and softened and became hardly palpable. This patient has had no *x*-ray treatment for twenty-two months, and has shown no evidence of spread of the disease. In view of the utter hopelessness and progressive course of such cases, these results are certainly of interest.

PRIMARY CARCINOMA OF THE BREAST.

Of course, *x*-rays as a method of treatment of primary carcinoma of the breast should never be undertaken when operation is feasible; but that something can be done in primary carcinoma of the breast is shown by postmortems that were made in two patients of mine who had been treated in this way. One case was a large primary carcinoma of the breast with involvement of the axillary glands and with spinal involvement at the time the treatment was begun, and treatment was only given on the family's insistence. The patient was referred to me by Dr. Wyllis Andrews. She had *x*-rays to the point of producing a dermatitis before she died. Postmortem, the breast was found a mass of connective tissue with little gland tissue and no carcinoma tissue left. The axillary glands had almost entirely disappeared and there was increase of connective tissue in their place. Another case of primary carcinoma of the breast was referred to me by Dr. J. B. Murphy. Three months after beginning treatment, Dr. Murphy wrote me concerning her: "The carcinoma of the breast has entirely disappeared." She died a short time afterward from acute illness, and postmortem it was found by Dr. W. A. Evans that the tumor had been converted into a small fibrous mass about the diameter and two-thirds the length of an index finger. The axillary glands had not been affected by the *x*-rays.

These findings warrant the attempt to treat by *x*-rays carcinomas of the breast in which, for any reasons, operation is out of the question; but they certainly do not warrant any one in advising *x*-rays as a substitute for operation.

Up to January, 1904, I had used *x*-rays in 15 cases of primary carcinoma of the breast. Of these 15 patients, 6 have died. Every one of these 6 was in an advanced stage of carcinoma, and absolutely hopeless; they were referred to me by men like Dr. Fenger, Dr. Wyllis Andrews, Dr. Murphy, and Dr. Ochsner. Seven of the remaining 9 are living, from one to three years after they came under treatment, and if the disease is still present, its extent has diminished very greatly and it has shown no tendency to increase. These were all comparatively favorable cases; none of them had ulcerated, but nearly all of them showed large tumors in the breast with retraction of the nipple and with involvement of the axillary glands. Concerning the diagnosis in these cases, I believe there can be no room for doubt. They presented characteristic pictures, and all of them had been pronounced carcinomas by competent men.

I do not know whether the two remaining patients are alive. These two were both old women with extensive ulcerating carcinomas, and there seemed no reason to hope for more than palliation. In one case

the ulceration was entirely healed and in both cases there was certainly decided improvement of the condition. Both the patients were living when I last heard from them, more than a year after they came under my observation.

I certainly do not believe that *x*-rays are entitled to any consideration as a reliable method for treating primary carcinoma of the breast, but, if operation is out of the question, I believe considerable hope of benefit, even of indefinitely prolonged relief, can be offered from *x*-rays.

CARCINOMA OF THE ABDOMEN AND OF THE PELVIS.

In carcinomas of the abdomen and of the pelvis, I have little that is definite to present. In carcinomas in the abdomen I have never convinced myself that anything has been done. In one case of carcinoma of the chest there has seemed to be very marked palliation from the use of *x*-rays. This was a case of carcinoma of the esophagus referred to me from Johns Hopkins by Dr. Halsted. Under *x*-ray treatment there was great improvement which was maintained for over a year. Then the tumor began to increase and killed the patient twenty months after he came under treatment.

I have treated several cases of recurrent carcinoma in the pelvis, usually after carcinoma of the uterus. I believe I correctly represent Dr. H. T. Byford and Dr. E. C. Dudley when I say that they thought there was considerable palliation in cases, which they observed, in the way of preventing vaginal involvement and perhaps in retarding the course of the disease. One such patient, referred to me by Dr. Byford, lived for one year in perfect comfort; her vaginal discharge and hemorrhage were quickly relieved and never returned; she was able to lead her usual life without inconvenience, and died within a week after the onset of her first acute symptoms. In another case, referred to me by Dr. Dudley, in which there was an enormous carcinoma extending well above the pelvis, the patient lived for one year without ever having a vaginal discharge and died within three days after she became bedridden.

The most radical improvement in any pelvic carcinoma that I have seen is in the case of a woman, referred to me by a Chicago surgeon. In October, 1903, after a history of hemorrhage beginning six months previously, the uterus and ovaries were removed for carcinoma. New nodules soon appeared in the scar which were treated assiduously after the usual methods, but continued to grow. At the time she came to me, on April 30, 1904, at the site of the vaginal scar there was a nodular mass about the size of a walnut, so large that it could not be entirely taken in by a Ferguson speculum. It was ulcerating and bleeding. In three weeks under *x*-ray exposures it had flattened down completely and there remained an ulcer the size of a ten-cent piece. In two months this had healed and left a healthy-looking scar. Since that time the patient has had one series of prophylactic *x*-ray exposures and she has remained well now for ten months. The vagina is perfectly clean and the scar is soft, without induration, and is healthy looking. The patient now weighs 175 pounds and is, as far as she knows, perfectly well.

SARCOMA.

My experience in sarcoma, of course, is not nearly so large as that in carcinoma, but it includes a considerable number of cases. The experience indicates that sarcomas are affected by *x*-rays in practically the same way as carcinomas. I am inclined to believe that they

are affected somewhat more readily. As the results, on the whole, are similar to those in carcinomas of similar extent, I will not burden this already overlong paper by an analysis of the cases. In general, it may be said that, as we rarely get sarcomas without the presence already of metastases, the results have been less favorable. Much can be done in way of palliation in many cases and symptomatic cures can be obtained in some.

PROPHYLACTIC USE OF X-RAYS AFTER OPERATION FOR MALIGNANT DISEASES.

The number of cases in which I have been able to carry out this procedure, while considerable, is not sufficient to allow of definite findings, and, as I have analyzed them elsewhere, I will not take the time to consider them here. This use of *x*-rays, I believe, is logical, and, as far as my experience extends, its utility is strongly confirmed by the results. I have a good many cases after operations for carcinoma and some after operations for sarcoma in which there are strong reasons for believing that the use of *x*-rays has thus far saved the patients. A few of the patients had had repeated operations for recurrences, and under *x*-rays have remained well now for a much longer time than any of the intervals between their previous recurrences. In a very few, the most desperate cases of this sort that I have treated, recurrences have taken place in spite of *x*-rays, but I believe I am correctly stating the impressions of the surgeons, who have sent me most of these cases, when I say that their record in the cases so treated seems to be better than it was before this became their practice.

It has been suggested many times that possibly the danger of the spread of carcinoma or sarcoma was increased when a lesion was exposed to *x*-rays. I have had this closely in mind, but in the several hundred cases that I have treated I have never seen a metastasis occur that seemed reasonably attributable to the use of *x*-rays. Metastases have certainly not occurred more frequently than would be expected naturally. I have, indeed, seen many lesions clean up without the development of metastases when there seemed to be every reason to fear them from the natural course of the disease. If this accident were probable it would show itself in my record of epitheliomas, and no such unexpected accident has happened in any of these cases.

PSEUDOLEUKEMIA AND LEUKEMIA.

The first suggestion, as far I know, of the use of *x*-rays in leukemia or in pseudoleukemia was made to me by Dr. A. J. Ochsner, and the first cases of this sort reported were three cases which I reported three years ago, two of which were demonstrated. One of these cases was a splenic leukemia which had inadequate treatment and was reported as a failure. The other two cases were cases of pseudoleukemia which I showed symptomatically cured. The first of these patients, a child 4 years old, had a recurrence of the disease in the neck seven months later, which was removed by operation, and the child died within a few days of inspiration pneumonia. In the second case, in which there had been very large glands, the patient is living and at his work at the present time. For two years after he was presented to the society he was well, he thought, and had no further treatment. A year ago he developed large mediastinal glands with pressure symptoms, but, much to my surprise, recovered under *x*-ray exposures given for a month. Recently he appeared again with

some glands the size of an olive in the neck and groins which have just disappeared under *x*-ray exposures. Except for these two months he has been in his usual health and vigor for three years. I have had several cases of pseudoleukemia which have cleared up under *x*-rays, but no other case that I have been able to follow so closely as this one.

My experience in removing the enlarged glands in true leukemia has been as favorable as in pseudoleukemia, but in most of the cases that I have seen the improvement in the blood has not kept pace with the decrease in the glands; while the patients improved, the results have not been radical. I have recently, however, had an extraordinary experience in true leukemia.

Patient.—A physician, aged 34, was referred to me on Oct. 3, 1904, by Drs. W. A. Evans and Adolph Gehrman with a diagnosis of splenic leukemia. He had not been in vigorous health for about a year, and on August 16 had had his appendix removed, and at that time his spleen was not enlarged.

Examination.—Soon after this he began to grow weak and five weeks later, on examination by Dr. Evans, he was found to have a well-developed splenic leukemia; it had developed, therefore, rapidly. On October 4 the spleen filled almost the entire left side of the abdomen, extending two inches below the umbilicus and inwards to the middle line, and was tender on pressure. The only other gland palpable was a pea-sized gland in the right clavicular space. He was much reduced in flesh and had rapidly lost strength until he was incapacitated for any exertion.

Blood.—The blood analysis of the Columbus laboratories at that time was as follows:

Percentage of hemoglobin	75
Number of red cells per cm.	4,080,000
Percentage of red cells	81.6
Corpuscle hemoglobin index	91.8
Number of white cells per cm.	160,000
Polymorphonuclears (per cent.)	58.6
Large mononuclears (per cent.)	10
Small mononuclears (per cent.)	4
Eosinophiles (per cent.)	1.2
Eosinophile myelocytes (per cent.)	1.2
Myelocytes (per cent.)	25

Treatment and Result.—The patient was given daily *x*-ray exposures, one over the spleen and a general exposure to take in all the body except the head. He was also given 10 mg. of sodium cacodylate, t. i. d. The improvement in his general condition was rapid. At the end of the first week he insisted that he felt distinctly better, and this improvement constantly continued. In two weeks the spleen was reduced to one-half its former size. On November 5, just one month after beginning treatment, the *x*-ray exposures were stopped on account of considerable erythema over the spleen, and he has had no further exposures, although the *x*-ray effect promptly subsided and at no time gave any trouble. By this time the spleen was reduced until it was just palpable. He had regained his normal health and vigor and had resumed his usual work. Since that time the general improvement and the improvement in his blood has been maintained. He has gained twenty pounds in weight, has a good color and the general appearance of a man in good health. The spleen shows no indications of returning enlargement and is not palpable.

Weekly differential blood counts showed continuous improvement until the blood became normal. Myelocytes were present in decreasing numbers until the middle of December, when they disappeared. At my request the Columbus laboratories made a count on December 28, which is as follows:

Percentage of hemoglobin	82
Number of red cells per cm.	4,736,000
Percentage of red cells	94.7
Corpuscle hemoglobin index	88.6
Number of white cells per cm.	6,900
Polymorphonuclears (per cent.)	73
Large mononuclears (per cent.)	6
Small mononuclears (per cent.)	19
Eosinophiles (per cent.)	2
Basophiles (per cent.)	1
Volume percentage	92
Coagulation firm in three minutes.	

GOITER.

I have used *x*-rays in a good many cases of goiter. In some small parenchymatous goiters there has been per-

manent diminution in their size. In one of these cases the gland has shown no returning enlargement after eighteen months. In most of the cases, however, there has been no benefit.

70 Madison Street.

A BACTERIOLOGIC AND CLINICAL STUDY OF A CURATIVE SERUM FOR TY- PHOID FEVER.*

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Although the production of an effective curative serum for typhoid fever would be a great addition to therapeutics, yet the accomplishment of this result is beset by several difficulties. It is well known that the typhoid bacillus is usually present in the blood and tissues, and that it increases in the tissues. The destruction of the bacilli in the circulation and tissues depends on the successful interaction of two distinct bodies.

The body which actually destroys the typhoid bacillus is the complement and is present as a ferment-like body in the serum or cells of the body. The second substance is usually the product of artificial immunity, though it too may be normally present in the body. It is well known as the intermediary body. Following out the theories of Ehrlich as so clearly explained by Welch¹ in the Huxley lecture for 1902, this intermediary body is produced in an immune serum by means of certain so-called haptophore groups which are possessed by the typhoid bacilli themselves. These groups of atoms have a special affinity for corresponding haptophorous groups in the cells of the body.

The continued appropriation of these receptors by the body cells causes an excessive production of similar receptors on the part of these body cells. Many of these are cast off into the lymph and blood and form the free amboceptors or intermediary body.

According to Ehrlich's latest statements, both the complement and the amboceptor, or intermediary body, are composed of several complex chemical groups. One group of the complement is called the zymotoxigenic group, and this causes the injury to the foreign cell which in the present instance is the typhoid bacillus. The complement also contains other groups which unite with complementophilic groups in the amboceptor, or intermediary body. The amboceptor in addition contains another haptophore group, which unites with a receptor of the foreign cell.

The destruction of the typhoid bacillus in the blood and tissues therefore depends on the assimilation of the zymotoxigenic group of the complement and the haptophore group of the intermediary body by receptors present in the typhoid bacillus.

EXPERIMENTAL WORK IN ANIMALS.

The work which we have undertaken has consisted in the production of a serum containing a large amount of the intermediary body, and it is therefore proper to

first consider the question of the efficacy of an immune serum in the treatment of experimental typhoid infection in animals.

It has long been known that the injection of nonfatal doses of typhoid bacilli into guinea-pigs will render these animals immune to further inoculations, and the mechanism of this immunity has been explained by the work of Pfeiffer, Metchnikoff and Ehrlich. These experiments have only resulted in the protection of normal animals against typhoid infection, and have still left the cure of infection an open question.

Abell and Loeffler² were among the first to demonstrate the power of immune serum to cure typhoid infection in animals, and the serum which they used was prepared by injecting fresh fluid cultures of the typhoid bacillus into dogs in gradually increasing doses. The bacillus which they used would kill guinea-pigs weighing 300 grams in doses of 1/50 of a cubic centimeter, but 0.001 c.c. of the immune serum would protect guinea-pigs against 100 times the minimum fatal dose in non-protected animals. They could also cure guinea-pigs infected with double the fatal dose of typhoid bacilli as late as eight hours after infection by injecting 0.5 of a cubic centimeter of this immune serum.

Ainley Walker³ also made a number of experiments which prove that animals can be protected against typhoid infection, and also cured after artificial infection has been produced.

In order to secure the maximum effect of a curative serum this writer considers that the animal yielding the serum should be injected with several different strains of *Bacillus typhosus*. This serum was prepared by first injecting a horse with dead carbolized cultures of one special strain of the typhoid bacillus. The dose was gradually increased to 150 cubic centimeters and this serum might be called serum No. 1. Serum No. 2 was prepared later from the same horse by injecting a similar mixture of four varieties of the typhoid bacillus, and it was therefore polyvalent. He found that serum No. 1 produced agglutination in much greater dilutions with the typhoid organism used for the immunization of the horse, than it did with the other typhoid bacilli. Serum No. 2, however, which was prepared by mixing the four different organisms, agglutinated all the types in much greater dilutions, although it still agglutinated the original bacillus in the highest dilution.

Rabbits were also immunized with races of bacilli from three different sources, and each strain was used for a definite period of time, one following the other.

It was found that the agglutinative power of the rabbit's serum rose toward each special bacillus during the period in which it was used for immunizing purposes, but remained much lower for other typhoid organisms.

The immunizing properties of the horse serum No. 1 and No. 2 were also tested by determining the least amount of serum which would protect guinea-pigs against the fatal dose of several different typhoid bacilli. Serum No. 1 was only protective in large doses when a type of bacillus was used which had not been used to immunize the horse. The polyvalent serum No. 2, in which four different types of typhoid bacilli were used for immunization of the horse, protected the

2. Abell and Loeffler: *Centralb. f. Bak. Erste Abt.*, Jan. 23, 1902.

3. Ainley Walker: *Antityphoid Sera*, *Journal of Path. and Bact.*, June, 1901; *Ibid.*, *Immunization Against Immune Serum*, *Jour. of Path. and Bact.*, March, 1902; *Ibid.*, *Production and Specific Treatment of Typhoid Infection in Animals*, *Jour. of Path. and Bact.*, November, 1901.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Fifty-fifth Annual Session, June, 1904.

1. Welch: *The London Lancet*, Oct. 11, 1902.