

Radium Treatment
in Diseases of the
Eye and Adnexa

By
C. J. BROEMAN, M. D.
CINCINNATI, OHIO

Reprinted from The Ohio State Medical Journal
April 1, 1925
Vol. XXI. No. 4
Pages 257-264

Herald Print, Batesville, Ind.

Radium Treatment in Diseases of the Eye and Adnexa.

By C. J. Broeman, M. D., Cincinnati, Ohio.

UNTIL a comparatively recent date it was generally believed that the ocular apparatus was particularly sensitive to the biological action of radium. At the present moment, however, this theory shows evidence of undergoing a change, this based on the actual experience of numerous men who have devoted their energies to this special line of work.

It seems to be a fact that the normal eye is influenced but little by the application of radium, for even when exposed for a considerable length of time, acute conjunctivitis (in some cases accompanied by temporary loss of eye-lashes) is the only untoward effect which, under skilled observation, may ensue.

Since prolonged radiation through this medium is known to exert an influence on all organs, tissues and cells of the body, this statement may appear illogical, but it has nevertheless been proved by actual experiment to be a fact. E. S. London¹ in 1911, in experimenting on both mice and rabbits, irradiating them for several months with 30 milligrams of radium bromide (about 15 milligrams of radium element), found that although there resulted ulcers of the skin, loss of sexual functions, loss of flesh and other constitutional impairment in various parts of the body, still as far as the eye was concerned, there occurred on the whole but slight change in the cornea and lens, although inflammation retina and optic nerves, and profuse secretion from the conjunctiva were generally found. Similar findings were the result of Birch-Hirschfeld's² thorough experimental study of the biologic influence of radium on the eye. A capsule containing 20 milligrams of radium bromide (10 milligrams of radium element) was fastened directly to the eye-lid of a rabbit. As a result of this experiment which lasted a few hours, the lens remained intact, while some alterations in the retina and optic nerve, dermatitis with

*Read before Eye, Ear, Nose and Throat Section, 78th Annual Meeting, Cleveland, May 13, 1924.

loss of hair, conjunctivitis and opacity of the cornea occurred. On the basis of these experiments, Chalupecky³ attached 5 milligrams of radium element in a mica-covered capsule to the eye of a rabbit, for from one to two hours, at first daily, then every other day, and followed this by a series in which there was an interval of several days. Following decapitation and microscopical examination of the animal, the following findings were set down: "The epithelium is irregular, with here and there a superficial loss of substance; the layers of the cornea are irregularly arranged, as if bent; a slight infiltration in the superficial layers and numerous small lacunae, as if the layers had been forcibly separated, in the remaining portions of the cornea an undoubted increase in fixed cells; no newly formed blood-vessels; Descemet's membrane uninjured. The iris and other parts are free from alterations; the lens is transparent and the retina of normal structure."

Probable Value of Radiation.

The probable value of radiation from radium elements as a therapeutic agent was, according to Williams⁴ first suggested by Williams Rollins of Boston, in 1900. Its application in the treatment of pathological conditions of the eye however, was first suggested by Dr. J. MacKenzie Davidson, in his introductory address to the Section of Radiology, British Medical Association, in July, 1910. This address was a summing up of Dr. Davidson's experience, and the hope was expressed that there be more extensive use of radium, as it had proved of great service, both in the treatment of external diseases of the eye as well as in diseases of the eye-lids. Much gratification also was voiced in regard to the absence of untoward inflammatory exacerbations or any other remote effects as a result of the application of radium. Thus, it will be seen, the use of these emanations in diseases of the eye have covered but a relatively short period of time; nevertheless, much work has been accomplished in this connection, and numerous valuable contributions to the literature have been made. Results of successful treatment as well as untoward results have variously been reported during this time, but it is the present writer's firm belief that success in the application of this therapeutic agent can only be attained as the result of long experience combined with persistent application of one who has specialized in

this branch of medicine, whether he be an ophthalmologist, dermatologist, general practitioner, or radium-therapist.

Although the writer is thoroughly experienced in the application of radium in diseases of the eye and adnexa, he wishes to emphasize the fact that he is not an ophthalmologist. This paper is a plea for the cooperation of the ophthalmologist, dermatologist and the radium-therapist. No cases have been treated by the writer except those which have been diagnosed by the ophthalmologist and, in turn, referred to him for irradiation. In addition, no treatment has been repeated unless the patient was again examined by the eye specialist and, in this way, continuous cooperation between the ophthalmologist and the radium-therapist has been established. Only by accurate diagnosis and the constant team work of men specially qualified in their various lines of work, can satisfactory results be attained. The ophthalmologist who has purchased a small amount of radium and who has not given radium therapy the necessary time and study can hardly be considered qualified to accomplish the results which will measure up to the standard of a radium-therapist who has given his undivided attention to its study and execution. We have all seen disfiguring results from the use of radium by an inexperienced operator or by the use of small quantities of radium when a large quantity was necessary to obtain the proper result.

One would naturally expect the dermatologists to be thoroughly experienced in the use of radium, since so many dermatological conditions of a superficial nature yield more readily to radium than to any other known therapy. Also one would expect the dermatologist to have efficiently treated, by radium therapy, many conditions on the eye-lids or other adnexa of the eye. And since there are a number of diseases of the eye that are amenable to no form of treatment except radium, one would expect a large percentage of eye specialists to be conversant with its therapy. In this connection it may be of interest to state that the writer sent out a questionnaire to six hundred men, including specialists in ophthalmology, dermatology and radium therapy, for the purpose of determining the exact status of the matter. As the result of the response, which was gratifying only numerically, the following deductions have been made: **firstly**, that radium,

in the treatment of ocular conditions, has been employed by only two per cent. of the ophthalmologists; **secondly**, that only one per cent. of the dermatologists have treated eye conditions; and **thirdly**, that only three per cent. of the men using radium to a degree have had any experience in treating conditions of the eye amenable to radium. It was surprising to learn that in conditions such as tuberculosis of the cornea, pterygium, and other conditions which respond well to radium therapy, only two or three men of the entire six hundred had had any experience with this form of therapy.

Conditions Amenable to Radium.

Among the conditions which the writer believes to be amenable to radium therapy are: xanthelasma, warts, angioma, molluscum (simplex and fibrous), carcinoma, trachoma, folliculitis, lupus conjunctivae, vernal conjunctivitis, tuberculosis of the conjunctiva, ulcers of the conjunctiva, benign tumors, epithelioma, sarcomata, melanoma, ulcers of gland, ulcers of the skin and lids, solid edema, eczema of the lids, keratitis, blepharitis squamosa (seborrhea), blepharitis ulcerosa (eczema), nevi cataract, blepharitis with hypertrophy of the border of the lids—truly a large range of pathological conditions.

Prior to reporting a number of cases treated with gratifying results, it may be well to summarize my ideas as to technique.

The treatment of disease of the eye and adnexa that respond well to radium treatment may be divided into two classes: (1) those that require superficial treatment, and (2) those that call for deep penetrating irradiation. There seem to be but a few conditions in the former class that can be treated with the superficial Beta radiation. The writer does not favor this form of treatment, as reactions tend to be more severe and are followed by more or less scarring and destruction of the tissues which later, become permeated with telangiectasis. If at any time it is found necessary to use the superficial Beta rays, it is advisable that never more than one-half doses is given at one treatment.

Among the conditions which have been attended with the most satisfactory results, in the writer's experience, is that of vernal catarrh. Failure to cure this condition, in many instances, is no doubt due to an error in diagnosis.

A history of the case is, of course, important and will prove of enormous value. The first report of a case of vernal conjunctivitis successfully treated by radium was that of Allport⁵ in 1903. Since then its treatment by this medium has been reported by various writers, and has been attended with some measure of satisfaction. In a report of several cases treated within a span of fifteen years Fusey's⁶ statement regarding the comparative value of Roentgen ray and radium is of interest. Although in his experience, results obtained with either X-ray or with radium were identical, the application of radium to the inner surface of the eyelids, he believes to be much less difficult than that of the X-ray. For this reason he has, in the last years, used only radium. He believes results to have been so gratifying in these otherwise intractable cases as to be worthy of a wider application than it had received up to that time.

The technique usually employed for vernal catarrh is the superficial Beta radiation. This can be given with the five or ten milligram radium plaque or with the bear needle or glass capsule. The plaque should be covered with a thin layer of rubber dam and applied over the mucosa of the upper and lower lid for from ten to twenty minutes. Personally, the writer would advise that it never be left in situ for more than ten minutes at one treatment. Where the eye-ball itself is involved, great care must be exercised, so as not to damage the cornea. Here the use of filtered radium would be preferable. The writer has found that in radiating cases of involvement of the upper and lower lids, enough rays are given off to take care of the ordinary involvement of the mucosa of the eye-ball. If, however, the mucosa is so badly involved that it needs special radiation, a tube in brass that is covered with rubber should, preferably, be employed. When the needle or glass capsule, or even the silver capsule, is used, the radium is held with a forceps and gently passed over the mucosa of the upper and lower lid, the upper lid being everted and held by a specially devised applicator, or strapped back with adhesive plaster.

In six cases of vernal catarrh treated by the writer, the lower lid was involved in only case, and to only a very slight degree. The treatment given above, when the plaque is used, may be repeated in a month or six weeks.

When the tube is merely passed over the lids, the treatment may be repeated as often as every week or two, until the desired result is obtained. It seems necessary, in most cases, to get some reaction before a cure is obtained. In the writer's experience, the reaction caused as a result of unfiltered radium has, in all cases, been more severe than when filtered radium was used.

Author's Technique.

In the treatment of the first cases of vernal catarrh, the writer used the ten-milligram plaque covered only with rubber dam and two layers of aluminum, thus following the technique most generally employed, namely, unfiltered radiation. The reaction being very severe, it was decided to use filtered radium instead. The following method has been used:

The patient lying on his back, a few drops of a two-per cent. solution of cocaine are placed in the eye; the lid is then everted, it being held in place with adhesive plaster. The ten-milligram plaque, one-half strength, with a 0.3 millimeter filter and rubber dam is then applied over the upper lid and held in place with adhesive plaster. If the case is a well-marked one of spring catarrh, the plaque is allowed to remain *in situ* for two hours. At the end of four weeks the patient usually has some reaction which lasts for a week or two. This treatment is repeated at the end of two months when, as a rule, all reaction has subsided. If, instead of the ten-milligram plaque a brass tube containing twenty-five milligrams of radium in silver, or the equivalent amount in needles, is placed in a brass tube, the technique and duration of treatment here has been the same as for the plaque, as the brass tube is always covered with a layer of vulcanizing rubber. Less reaction has been noted with the tube than with the plaque, and it may require one-half hour more time with the tube than with the plaque. It usually takes from four to six applications, such as described here, to effect a permanent cure. The writer has never failed to cure a case of vernal catarrh by this method, and finds sufficient encouragement for continuing to employ the filtered radium.

Advantages of the Unfiltered Radium Technique.

First: Less time is required to treat the patient.

Second: It is not necessary to give the patient a

room, and your radium is at your disposal for the treatment of other cases.

Third: Perhaps a quicker result is obtained.

Disadvantages of the Unfiltered Radium Technique.

First: Patients must come to the office every week or two. This is hard on the out-of-town patients.

Second: Reactions are apt to be quite severe and it may leave considerable scarring and disfigurement.

Third: The ultimate end-result does not seem as perfect or uniform as when the filtered radium is used, as you do not get as uniform a reaction as when the filtered radium is allowed to remain in one position.

Disadvantages of Author's Filtered Radium Technique.

First: It probably takes a little longer time to cure the patient.

Second: This method may produce a temporary loss of eye-lashes. This happened in only one case, and it was not permanent.

Third: The necessity of having a room for the patient to lie in for several hours.

Advantages of Author's Filtered Radium Technique.

First: Patients have to report to the radium therapist only once in two months.

Second: This is of much benefit to the out-of-town patients.

Third: Reactions are less severe and there is very little danger of scarring or deformity in the ultimate end-result.

Deep-Seated Conditions.

Deep-seated conditions of the eye-ball or any malignant conditions of the eye-ball or surrounding tissues should first be treated with well-filtered radium application. In rare instances it will be found that it is necessary to use an unfiltered application if the condition is on the lids, and instance of this is an epithelioma or warty growth of the lids. Also in xanthoma, the superficial treatment has been found to be of much benefit.

Conditions Treated by the Writer.

Among the conditions treated by the writer, which have been attended with success are vernal catarrh, pemphigus of the eye-lid, sarcoma, round-cell sarcoma,

xanthoma palpebrarum, blepharitis, solid edema of right orbital cavity, sarcoma of the retina, sarcoma mucosa of right upper lid, sarcoma of right eye-ball, sarcoma of right orbit (postoperative), epithelioma of both upper and lower lids, papilloma of the cornea, trachoma, melanotic sarcoma of the right cornea, moles, benign growths, trachoma and pamsis, chronic ulcer of right upper-lid, granuloma of the iris, iritis, glaucoma, melanotic sarcoma of the left orbit, chronic eczema of the outer canthus of both eyes, papilloma of the lids.

Case Reports.

Pterygium.—Case 1. Mr. S. M., age 45; referred by Dr. D. T. Vail.

Diagnosis: Dec. 30, 1920—Pterygium left cornea beginning malignancy.

Treatment:

Dec. 30, 1920—Radium plaque 0.3 brass, lead shield, for 2 hours.

Jan. 4, 1921—50 milligrams brass rubber, for 2 hours.

Jan. 17, 1921—50 milligrams brass rubber, for 3 hours.

Feb. 14, 1921—Much improved.

March 2, 1921—50 milligrams brass rubber, for 3 hours.

Remarks: Feb., 1924, patient reported well with no recurrence.

Solid Edema Right Orbit.—Case 2. Mr. H. W., age 42; referred by Dr. D. T. Vail, Jan. 23, 1922.

Diagnosis: Solid edema right orbit. Seven years' duration.

Treatment: 50 milligrams brass, $\frac{1}{2}$ inch felt over left eye, for 6 hours.

25 milligrams brass, $\frac{1}{2}$ inch felt over right eye, for 6 hours.

25 milligrams brass, $\frac{1}{2}$ inch felt left upper lid for 6 hours.

Remarks: This condition began seven years ago in the left eye and in the last year began to develop in the right eye.

This rare condition was the second case that Dr. Vail had ever seen and the first case that came under the author's observation.

The treatment was entirely experimental and was a perfect success, as a letter from the patient Feb. 12th, 1924, states that he is entirely well.

Papilloma Cornea.—Case 3. Mr. W. E. R., age 72; referred by Dr. Wylie McLene Ayres, March 17, 1921.

Diagnosis: Papilloma cornea.

Treatment:

March 17, 1921—50 milligrams brass rubber tubing across the eye, for 1 hour.

March 29, 1921—50 milligrams brass rubber tubing across the eye, for 1½ hours.

April 7, 1921—50 milligrams brass rubber tubing across the eye, for 2 hours.

April 14, 1921—25 milligrams across the eye, for 1½ hours.

April 28, 1921—10 milligrams radium plaque 0.3 brass filter across the eye, for 2 hours.

May 31, 1921—50 milligrams brass rubber across the eye, for 3 hours.

June 20, 1921—25 milligrams brass rubber across the eye, for 1½ hours.

July 17, 1921—Slight conjunctivitis.

July 25, 1921—25 milligrams brass rubber across the eye for 1½ hours.

Aug. 15, 1921—Mild reaction.

Remarks: This condition while reduced to one-third its size was not cured by radium, and an operation was advised.

Two similar conditions received through radium treatment with the same results, that is, a reduction in the size of the growth but not a complete cure in any sense of the word. It is the writer's belief that true papilloma of the cornea without any malignant change is not amenable to radium therapy; however, if the growth is undergoing epitheliomatous changes, radium is of distinct benefit. Radium is also of benefit in preventing recurrence of the growth.

Eczema of Right Eye-Lid.—Case 4. Mrs. E. L. H., age 35; a former patient, presented herself on October 31, 1922, with a chronic eczema of the right upper eye-lid. This condition failed to yield to the usual form of treatment.

Treatment:

25 mg. tube of radium on $\frac{1}{4}$ inch felt was applied over the lid for 2 hours. This form of treatment cured the condition in two months without any recurrence.

Vernal Catarrh.—Case 5. Master W. L., age 14 years; referred by Dr. D. T. Vail, Jan. 29, 1921.

Diagnosis: Vernal catarrh both upper lids.

Treatment:

Jan. 29, 1921—10 mg. radium plaque, two layers of aluminum, 40 minutes over each everted eye-lid.

Feb. 10, 1921—Same treatment repeated. Left eye-lid 30 min. Right eye-lid 20 min.

March 11, 1921—Same treatment repeated on left eye-lid, for 25 min.

April 9, 1921—Radium plaque with 0.3 millimeter brass filter over left lid, for one hour.

April 30, 1921—Same treatment repeated on left lid only. 50 mg. radium tube silver and brass, covered with vulcanizing rubber over right eye, for 40 minutes.

June 2, 1921—Radium plaque 0.3 millimeter brass filter, over left upper lid, 2 hours. 25 mg. radium tube, in silver and brass covered with vulcanizing rubber over right upper lid, 45 minutes. 25 mg. silver only, right corner bottom right eye, 10 minutes. Same treatment left corner right eye, 10 minutes.

August 25, 1921—Patient was again at office, and had improved very much.

Remarks:—Reaction after the first two treatments was quite severe, but following that the reaction was slight. In the summer of 1922 the eyes had improved to such an extent that the boy was able to attend Culver College, spending the entire day out in the sun, horseback riding, swimming, etc.

Vernal Catarrh.—Case 6. Master H. M., age 17; referred by Dr. Henry Stanbery, March 1, 1921.

Diagnosis: Vernal catarrh of the upper and lower lids with eye-ball involvement.

Treatment:

March 1, 1921—Here we used 10 mg. radium plaque with two thin layers of aluminum. This was laid over the eye-ball for 6 minutes and the upper and lower lids

for 25 minutes each. The reaction 10 days later was quite severe.

April 4, 1921—10 mg. radium plaque, two layers of aluminum over right and left lid, 20 minutes each.

May 28, 1921—Two radium needles covered with vulcanizing rubber in left corner of the left eye, one hour. Radium plaque 0.3 millimeter brass filter over right eye-lid, 1 hour.

June 27, 1921—25 mg. radium tube covered with vulcanizing rubber, right eye-lid 1½ hours. Same treatment over left eye-lid.

Aug. 5, 1921—Radium plaque 0.3 millimeter brass filter over right eye-lid 2½ hours. 25 mg. tube silver and brass covered with vulcanizing rubber over left eye-lid, 2½ hours.

Sept. 21, 1921—Same as above.

Nov. 21, 1921—Same as above.

Remarks: This boy's eyes were in a very bad condition; it was the worst case the writer has ever treated. The boy had not gone to school for years. Treatment extended from March 1 to November 21, 1921. At this time he was pronounced well and had been going to school for quite a while.

Vernal Catarrh.—Case 7. Master C. B., age 6 years; referred by Dr. D. T. Vail, September 13, 1921.

Diagnosis: Vernal catarrh.

Treatment:

September 13, 1921—25 mg. radium needles over right eye-lid ½ hour. (Needles were in silver and brass.) 10 mg. radium plaque, 0.3 millimeter brass filter over left eye, ½ hour.

October 26, 1921—10 mg. radium plaque 0.3 millimeter brass filter, right eye, 2 hours.

25 mg. radium tube in silver and brass covered with vulcanizing rubber over left eye, 2 hours.

October 31, 1921—First reaction. Condition improved.

November 14, 1921—Two 25 mg. radium needles in silver and brass, 1 hour, 15 minutes, over right eye. 10 mg. radium plaque 0.3 millimeter brass filter, left eye, 1 hour, 45 minutes.

January 13, 1922—10 mg. radium plaque 0.3 millimeter brass filter, left eye, 2 hours.

May 16, 1922—Plaque 0.3 millimeter brass filter over right eye, 2 hours; over left eye, 2 hours.

Vernal Catarrh.—Case 8. Master R. B., age 11 years; referred by Dr. Fred. Lamb, February 2, 1923.

Diagnosis: Vernal catarrh, well marked on both upper lids with slight involvement of the lower lids. Condition present three or four years. Usual symptoms of photophobia present.

Treatment:

March 1, 1923—10 mg. radium plaque 0.3 millimeter brass filter and rubber dam was applied to the upper lids for 2 hours. 25 mg. tube in silver and brass and covered with vulcanizing rubber was applied to the lower lids for one hour each. Sixteen days later patient had a mild reaction.

April 21, 1923—Same treatment was repeated, except that it was not found necessary to treat the lower lids, two hours being the length of the treatment.

June 7, 1923—Two 25 mg. radium tubes, in silver and brass and covered with vulcanizing rubber were applied for one hour each on the upper lids. At this time the patient was greatly improved.

September 7, 1923—Similar treatment was given.

November 15, 1923—Patient practically well. A 25 mg. radium tube, silver and brass, covered with rubber over each upper lid, 1 hour each.

Remarks: In all of these cases of vernal catarrh we have found that dropping a few drops of 2 per cent. cocaine solution into the eye and holding the everted lids in place with adhesive plaster was as good a method as any.

Pemphigus.—Case 9. Mr. C. K., age 37 years; referred by Dr. D. T. Vail, October 30, 1922.

Diagnosis: Pemphigus of right eye.

Treatment: 25 mg. radium tube in silver and brass on $\frac{1}{4}$ inch of felt was placed over the closed eye for $2\frac{1}{2}$ hours. Two months later the same treatment was repeated for $3\frac{1}{2}$ hours.

Remarks: This condition disappeared without any reaction, even the eye-lashes did not fall out.

Sarcoma Mucosa Upper Right Lid.—Case 10. Mr. J. S., age 58; referred by Dr. H. B. Diekmeier, January 16, 1922.

Diagnosis: Sarcoma of the mucosa of right upper

lid, with secondary involvement of the parotid glands and cervical glands on the right side.

1st Treatment: Jan. 17, 1922—50 mg. radium tube in silver and brass covered with vulcanizing rubber over right upper lid, 2 hours.

(Six treatments in all were given to these different areas.)

2nd Treatment: Jan. 18, 1922—Two 25 mg. radium needles were used instead of the 50 mg. radium tube, for 3 hours.

3rd Treatment: Jan. 24, 1922—Same as above.

4th Treatment: Jan. 26, 1922—50 mg. tube was used. 100 mg. radium were used on right side for 5 hours.

5th and 6th Treatments: These treatments were practically the same.

Remarks: The diagnosis of sarcoma was confirmed by microscopical examination which reported round-celled sarcoma. At the present time patient is living and well.

Chronic Ulcer of Right Upper Eye-Lid.—Case 11. Master G. B. H., age 11 years; referred by Dr. D. T. Vail, June 20, 1923.

Diagnosis: Chronic ulcer of right upper eye-lid.

Treatment: 25 mg. radium tube in brass and silver placed on $\frac{1}{4}$ inch of felt, applied over the affected area for 2 hours and 15 minutes.

Remarks: One treatment resulted in a perfect cure. No reaction whatsoever.

Xanthoma Palpebrarum.—Case 12. Mrs. K. B.; referred to the writer March 25, 1922.

Diagnosis: Xanthoma palpebrarum.

Treatment:

March 25, 1922—10 mg. radium plaque 0.3 brass filter, for $1\frac{1}{4}$ hours.

April 1, 1922—10 mg. radium plaque 0.3 mm. brass filter, $1\frac{1}{2}$ hours.

April 8, 1922—10 mg. radium plaque 0.3 mm. brass filter, $1\frac{1}{2}$ hours.

April 15, 1922.—10 mg. radium plaque 0.3 mm. brass filter, 1 hour.

April 29, 1922—Mild reaction.

Remarks: Areas treated with radium with a fairly satisfactory result.

Melanotic Sarcoma.—Case 13. Mr. F. W. M., age 43 years; referred by Dr. G. Hinnen, May 5, 1921.

Diagnosis: Melanotic sarcoma of right cornea and mucosa of the lid,

Treatment:

May 14, 1921—25 mg. radium tube in silver and brass covered with vulcanizing rubber applied over the area, 1½ hours.

May 18, 1921—two 12½ mg. radium needles in silver and brass, covered with rubber, 3 hours.

May 22, 1921—Same treatment repeated.

May 28, 1921—Reaction.

June 25, 1921—Same treatment.

Aug. 7, 1921—25 mg. tube in brass and silver, 2½ hours.

Aug. 21, 1921—Reaction.

Sept. 26, 1921—25 mg. tube.

Remarks: On February 12, 1924, patient reported well, with no recurrence.

References:

1. London, E. S.: *Das Radium in der Biologie und Medizin.* Leipsig, 1911.
 2. Birch-Hirschfeld: *Arch. f. Ophthal.*, vol. 59.
 3. Chalupceky, H.: *The Action of Radium and Radium Emanation on the Visual Apparatus.* *Wien. klin. Rundschau*, No. 52, Dec. 24, 1911. Transl. by Adolph Alt. *Amer. Jour. Ophth.*, Vol. 29, No. 1, pp. 10-17, Jan. 1912.
 4. Williams, Francis H.: *Early treatment of Some Superficial Cancers, especially Epitheliomas by Pure Radium Bromid rather than Operation or X-rays.* *Jour. Amer. Med. Assn.*, Vol. 51, pp. 894-897, Sept. 12, 1908.
 5. Allport, Frank: *A Case of Vernal Conjunctivitis.* *Ophthal. Rec.*, Vol. 12, No. 10, pp. 484-487, Oct., 1903.
 6. Pusey, William Allen: *Treatment of Vernal Conjunctivitis with Radium.* *Jour. Amer. Med. Assn.*, Vol. 71, pp. 806-807, Sept. 7, 1918.
- 4 West Seventh St.

Discussion.

D. T. Vail, M. D., Cincinnati: An eye case is occasionally met with that seems to resist every available treatment at our command. Indeed our treatment often aggravates the condition. Cases of spring catarrh belong to this class, also some cases of trachoma that are in the latter part of the second stage of the disease where there is a great deal of thickened tissue and much scar formation but not many fresh trachoma follicles; likewise pemphigus of the lid margins, certainly a baffling disease

by any line of treatment with the medicaments with which we are familiar.

Then too there is a small group of cases which we have been accustomed to handle by operative procedures. Cases of epitheliomata of the eyelids belong to this class. Many in this group are well and successfully treated and cured by excision. Such a surgical procedure very often taxes our ingenuity to perform in a way that will not result in unsightly scar formation, ectropion or interference with the function of the tear drainage apparatus.

My rule of action in these cases before the days of radium was, to excise heroically all diseased tissue well beyond the apparent border of affection regardless of deformity and then at the same seance resort to plastic surgery; sliding flaps or transposing skin to render as good a cosmetic result as possible. Too often the cosmetic idea was lamely carried out but it was regarded satisfactory if there was no recurrence of the growth.

Epithelioma of the eyeball is another affection of more serious nature which threatens not only the welfare of the eyesight but also the life of the patient after months of frightful suffering with the slowly progressing ulceration of tissue and the hideous deformity. These patients usually come to us early when the growth is small and we operate with the hope of a cure. In them I have adhered to the principle mentioned above, viz., operating radically to remove every visible vestige of diseased tissue regardless of consequent deformity and finishing the operation by almost unwarranted use of the galvano cautery. While I confess that the results of this kind of surgery have been usually gratifying, the scar formation and deformity have in many cases been rather objectionable to say the least.

There are certain semi-malignant rather rapidly-growing soft and sometimes hard growths that occur in the anterior orbital and peribulbar tissues that have so insinuated themselves between and around the recti and oblique muscles that the surgical idea is difficult or impossible to carry out without maiming the muscles and producing annoying consequences. They are cylindromata, myxomata, fibromata and other such tumor masses. Some will produce exophthalmos, others create visible and rather rapidly-increasing tumors that present in the culdesacs or eyelids and they are not pleasant to deal with from a surgical standpoint.

All these groups of cases and a few others are now well treated and most are magically cured by the proper application of radium. The cases Dr. Broeman has reported and shown on the screen illustrate in a convincing manner that we have in radium a plan of treatment to propose to patients afflicted with any of the maladies mentioned in these groups which is not only the most promising in end results but far less annoying to the patients.

It is therefore now possible to regard these cases in a new and altogether more favorable light. I have found

it a pleasure to get rid of all such cases by referring them to a radium expert and by so doing I feel that I am rendering such afflicted patients a valuable service.

In order to meet with success the radium expert must not only know how to apply radium but he must have a sufficient amount of the right kind and he should have it in various shapes and forms. Radium is very expensive, the use of it calls for expert knowledge and proper training. Radiology is a specialty per se. Each city should have one, two or even a greater number of radium specialists to whom we may refer cases suitable for radium therapy. We cannot very well install a radium department in our own offices. We have not a sufficient number of suitable cases for radium treatment to make it worth while.

Dr. Broeman has mentioned some cases I have referred to him and it may be well to say a few words regarding the clinical features they exhibited when they came to me.

Case I. C. K. with pemphigus of the right eye-lids presented the clinical picture of a very chronic and aggravated case of blepharitis marginalis. He had been treated for this trouble by three of the best ophthalmologists with no benefit. His left eye-lids were free from disease. I employed the most thorough and painstaking local treatment to the margins of his affected eyelids without any satisfactory results. I then diagnosed the condition blastomycosis of the eyelids and put him on large doses of iodide of potash inwardly. There was no appreciable benefit and so I changed the diagnosis to pemphigus of the eyelids, told him I could not cure him and I advised him to try the radium treatment referring him to Dr. Broeman. Broeman states he is cured. If so, it is most remarkable, being the first case of pemphigus of the eyelids I have ever seen cured.

Case II.—Master G. H., my diagnosis of the eye affection in this patient was chancre of the eyelid. I referred him to Broeman as a dermatologist who would treat him for the systemic as well as the local trouble. Broeman diagnosed chronic ulcer with mixed infection and cured with radium.

Case III. S. M. had the most marked ectropion of both lower eyelids I have ever seen. He also had what I diagnosed as a malignant pterygium of the left eyeball. This growth had been treated surgically several times by others. I corrected the ectropion by operation achieving an ideal result and referred him to Broeman for radium treatment of the apithelioma or malignant pterygium. I saw the patient afterward. The cure seemed complete.

Case IV. Mr. H. H. W. had noticed for seven years a "lump" in the lower culdesac of the left eye. He noticed it was slowly getting larger but there was no inflammation and no unpleasant symptoms and so he paid no attention to it. Six months ago he discovered a similar swelling in the lower culdesac of his right eye. When he

came to me there were conspicuous swellings of both lower eyelids. The tumors seemed indurated to the touch. Upon everting his upper eyelids I discovered similar growths presenting in the upper culdesacs. I diagnosed solid edema of the eyelids and referred him to Broeman as my surgical experience with solid edema was not pleasant. He was cured with radium.

Cases V. and VI. W. D. L. and C. B., boys aged fourteen years, six years respectively. They both exhibited the most pronounced objective and subjective symptoms of vernal catarrh of the conjunctiva. The tumors were like mucous warts and occupied the entire area of the tarsal conjunctiva of both eyelids in both eyes. The patients were not greatly annoyed during cool or cold weather but in hot weather the itching, discharge and lachrymation were intolerable. They had each been treated by excellent ophthalmologists with no relief.

I frankly told the parents I could not cure the disease and advised them to see Broeman. These boys were both entirely cured by radium emanation.

Dr. Broeman did not mention several patients affected with small epitheliomata of the eyelids which I referred to him and which were promptly cured with radium.

I am waiting to learn the result of his treatment of a vicious case of trachoma in both eyes of a boy aged eighteen, recently referred to him. This young man has had his lids operated upon twice and as a consequence there is much scarring and the trachoma condition is, if anything, worse than before. Pannus is pronounced. He is practically blind.

I can truly say that according to my observation of results of radium treatment in a rather large number of cases referred to Dr. Broeman and to Dr. Goosman that the remedy is most valuable, that the results of its proper application in suitable cases are magical leaving as a rule no visible scar or deformity and that radium has proved a Godsend to those afflicted with certain ocular diseases hitherto incurable.

F. G. Slueber, M. D., Lima: Dr. Broeman is to be congratulated upon the fine results with radium therapy. His paper, and Dr. Vail's discussion are of much interest.

We are pleased to see that some satisfactory results are obtained in vernal catarrh, also note its usefulness, in pterygium, trachoma, follicular conjunctivitis, ectropion, new growths and external eye diseases in general.

Just what may be achieved in glioma and malignancy in general remains for the future to determine. Some authorities caution against too long exposure in order to safeguard nerve and retina. No doubt those skilled in radio therapy have some manner of control so that deeper structures and dangers thereto, may be reduced to a minimum.

Office and Private Hospital
4 West Seventh Street.

RADIUM



By C. J. BROEMAN, M. D.

Cincinnati, Ohio

Ass't Director, Dep't Dermatology and Syphilis, Cincinnati Gen'l Hospital, Medical Department, University of Cincinnati; Visiting Dermatologist St. Mary's Hospital, Episcopal Hospital for Children, Instructor in Syphilis and Dermatology, Ohio College of Dental Surgery, Etc., Formerly Ass't Surgeon, Dept. Venereal Diseases, United States Public Health Service.

Reprint from the Kentucky Medical Journal,
June, 1921.

RADIUM

Every new discovery, when its value is put to a practical test, finds enthusiastic supporters and equally ardent detractors. Some of the physicians who are employing radium have no doubt become over-enthusiastic about its value putting it forward as a universal panacea because some most unexpected and remarkable results have followed its employment, but nevertheless, the fact remains that radium is here to stay, and moreover, has a field in medicine separately and peculiarly its own, a field which drugs or surgery or x-ray therapy can never occupy. It, therefore, behooves every physician to inform himself concerning it, even if he has no intention of making use of it personally, for the public interest has been so much aroused by the reports concerning radium, which have appeared in literature and the accounts of the almost miraculous results which have at times followed its application, that the medical man who is not armed with exact information concerning it may be put in a position of great embarrassment by the first inquiring patient who questions him about it.

Perhaps the most frequent question he will encounter will be: How much is it going to cost? Owing to the great scarcity and consequent high price of the element there is a popular impression that radium treatment is very expensive. This is far from being the truth. Even when one considers the cost of the mechanical equipment—which is considerable—and the special training required before one can become a competent operator, these initial costs are more than offset by the fact that the treatment seldom requires an extended sojourn in the hospital, as in many cases it can often be administered in the physician's office. As the applications are absolutely painless it is frequently possible for the patient to receive them without interruption of his regular employment, which is, of course, out of the question if a surgical intervention is undertaken. When these considerations are taken into account it will be seen that the patient should be able to pay a reasonable fee for his treatment without assuming an overwhelming financial burden.

Physics of Radium.

"Radio-activity is the power of spontaneously sending out rays which penetrate through all forms of matter, affecting photographic plates in darkness and discharging electrified bodies." Radio-activity was discovered twenty-four years ago by Becquerel, a French physicist, while he was working with uranium oxide. Two years later, in 1898, Madame Curie discovered a radio-active substance possessing an activity several million times greater than uranium. This, she called radium. It is found in a number of radio-active ores, such as pitchblende-uranite, chalcote, thoramite and carnotite. Carnotite is mined

in Colorado and is the only source of radium in the United States. Uranium exists in it in a proportion of about two per cent, and from this radium is extracted, about thirty-five tons of ore being required to furnish one hundred milligrams of radium element. There are about three ounces of radium now in existence, and each ounce is valued at \$3,402,000.00.

When we speak of using so much "radium" it is not the element itself which is referred to, but one of its bulkier salts or its gaseous emanation. The purchaser of a hundred milligrams of radium receives it in the form of radium bromide or chloride (soluble) or sulphate (insoluble) just as though the purchaser of a dram of metal sodium



Epithelioma upper and lower lids of right eye, involving inner canthus.

should receive an equivalent amount of sodium chloride or common salt. One milligram of the element corresponds to 1.87 milligrams of the bromate, 1.31 of the chloride, 1.265 of the carbonate and 1.42 of the sulphate. The yearly decay is three-one-hundredths of one per cent; that is to say, in one thousand, seven hundred and fifty years radium will lose one half of its strength and at the end of twenty thousand years virtually none of it would be left.

Emanation may be termed the "vital spark" of radium. It is an element formed of radio-active matter, but it must be remembered that it is not a ray. When it transmutes (changes) it gives off an Alpha ray. The life of the ema-

nation is much shorter than that of radium itself, as half of any quantity of emanation decays in 3.85 days, and the remaining half in an equal space of time, so that at the end of forty days only a minute quantity will remain. During the decay process each of the decay products gives off rays.

There are three kinds of radium rays, Alpha, Beta and Gamma, named after the first three letters of the Greek alphabet. The Alpha rays constitute 90 per cent of the total radium energy. They have a velocity of 12,000 miles a second—which is one-twentieth the velocity of light—but they are very easily cut off with a “screen” or “filter” such as a sheet of paper, and can travel through the air a distance of only thirty-three centimeters. Because of



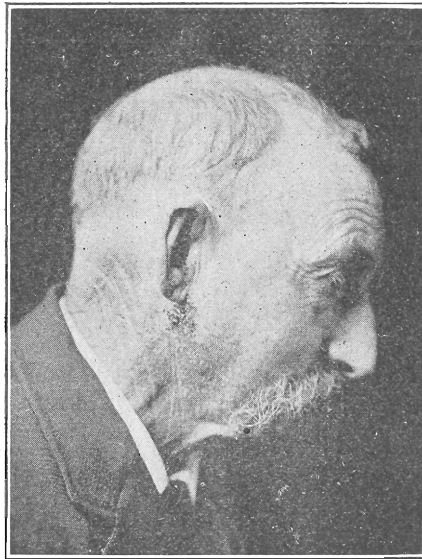
Three months later, having received 550 mg. hours of radium treatment. Apparently cured.

the enormous energy with which the Alpha rays are shot out from the transmuting atom, they produce the greatest heating effect of the three kinds of rays, furnishing 123.6 of the total of 134 calories produced by one gram of radium in one hour. The Alpha rays are the least penetrating of the three.

The Beta rays are one hundred times more penetrating than the Alpha, and their velocity is much greater, being the same as light. They constitute about nine per cent of the total energy of radium. They are almost completely absorbed by a thickness of eight millimeters of aluminum or two millimeters of lead. The Beta rays are the true “burning rays” for unless the surface which is

to be irradiated is protected by lead, aluminum, brass, silver or rubber, long exposure to them will produce characteristic burns. There the three kinds of Beta rays, soft, medium and hard, the last named being the most penetrating.

Gamma rays are one hundred times more penetrating than Beta. Although analagous to x-rays produced in a hard vacuum tube, they are much more penetrating, as they will pass through a man's body at the level of the thorax and illumine a radiosopic screen on the other side. After passing through one centimeter of lead about 40 per cent of the Gamma rays will be absorbed, and when ten centimeters have been passed through 0.6 per cent



Epithelioma of the neck just beneath the lobule of the right ear;
duration two years.

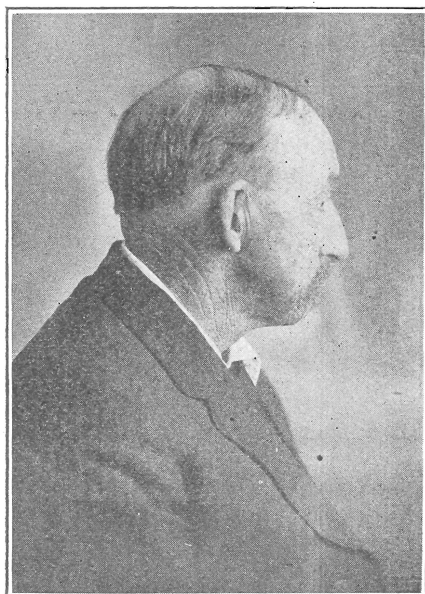
will still be unabsorbed. The Gamma rays which encounter matter, either tissues or the screen, develop into secondary Beta rays. In medical work the Gamma rays is the most important as it has a selective action upon diseased cells. As its penetration is in a direct line the applicator must be placed parallel to the part to be treated.

Technique.

The physician working with radium can secure the best results by co-operating with those who have made a special study of the region which is to be irradiated. I never attempt to treat disease of the nose or throat without con-

sultation with a laryngologist, so that I may be certain that the radium is placed exactly where it should be. In the same way when dealing with a difficult uterine condition I have sought the help of a competent gynecologist. Care in placing the radium is one of the very important factors influencing the outcome of the treatment, and all dosage must be adapted to the requirements of the individual patient and the amount carefully calculated by the operator. Success is largely dependant upon attention to these details.

Radium is applied in several ways: By means of flat applicator or plaques; in tubes; by means of needles or



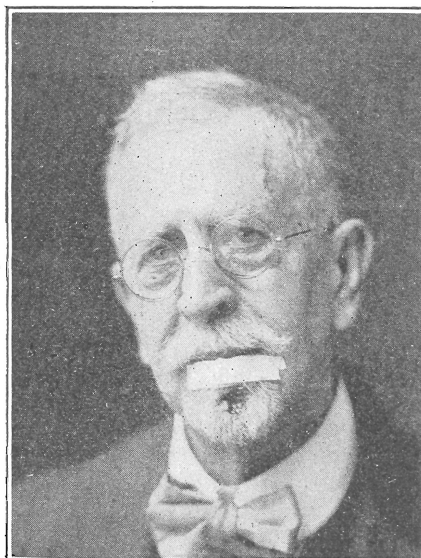
Three months later. Apparently cured after 1200 mg. hours of radium treatment.

by glass capsules in which the radium emanation is sealed up and used in place of the element itself.

The flat applicators designed for dermatological work may be of any desired size or shape, but the usual form is a metal plaque from one to four centimeters square, over which the radium is evenly distributed after being mixed with a suitable varnish or enamel. Sometimes the radium is first enclosed in aluminum, so that, should the enamel be cracked or chipped, the radium would not be lost. This aluminum will absorb the Alpha rays. The screens most commonly used for the plaques are squares of aluminum, brass or lead, varying in thickness, that of the brass being from 0.3 to 2.0 mm. Plaques are sometimes

ten severe and very painful. This is especially likely to occur in cases where the patient has had several treatments of large applications close together, so that he experiences what might be termed an accumulative reaction.

This reaction is manifested in one of four degrees: (1) Erythema, (2) erythema with desquamation, (3) vesication with superficial ulceration and (4) deep ulceration. All tissues treated with radium react in some way, the manner of this reaction depending upon (1) the apparatus, screening and dosage employed (2) the nature and condition of the tissue treated, (3) the extent of the application and (4) personal idiosyncrasy of the patient. Ordinarily the reaction is characterized by an increased

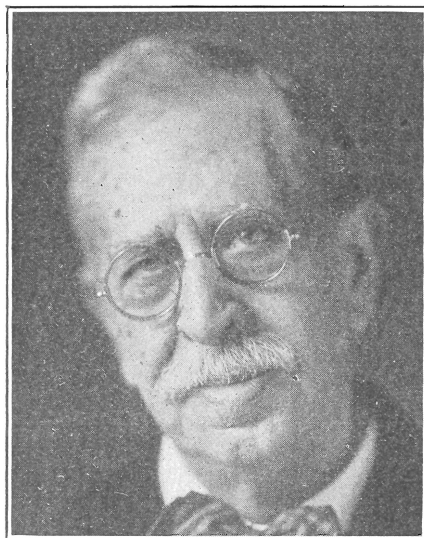


Epithelioma of the chin: duration twenty-four years: also epithelioma under left eye; twelve years duration.

hyperemia of the skin, occurring about ten days after the application, followed by the shedding of the epidermis and formation of a vesicle. In about twenty days an ulcer will form under a crust, which falls off in four or five weeks, leaving a cicatrix which is depigmented, hairless, smooth and supple.

In the employment of radium it must always be remembered that it is a very powerful agent and that much care and study in addition to experience are necessary for its successful use. Not only must the operator have a comprehensive understanding of the action of the rays, but also he must acquire an exact knowledge of the activity of his plaques and tubes. Likewise he must have

a thorough knowledge of the disease or condition he is trying to cure. The basal-celled epithelioma must be treated quite differently from the prickle-celled type, plaques being used for the basal-celled while the treatment of the prickle-celled necessitates the employment of tubes. One patient will react more severely and quickly to the action of the radium rays than will another. One who is suffering from a chronic localized patch of eczema usually reacts in a comparatively short time and to a marked degree, such skin blistering and becoming irritated much sooner than normal skin. Strange as it may seem, a large tuberous naevus will do beautifully under radium, while a spider naevus cannot be treated with radium at all. This



Three months later: 700 mg. hours to chin; 500 mg. hours to epithelioma under left eye. Both apparently cured.

is because the spider naevus contains no naevus tissue, nor any hyperplastic naevus blood vessels which can be acted upon by the Gamma rays. The dilated central point and the radiating capillaries are easily obliterated with the electrolytic needle.

Method of Administration.

There is every reason to believe that the next ten years will see a great reduction in the present high mortality rate of cancer through the application of radium. At present this disease yearly exacts a toll of ninety thousand lives, the mortality being particularly heavy among women over forty, as the female genital organs are especially suscep-

tible to attack by it. In the field of gynecology radium can be used to the greatest advantage.

An intra-uterine application of fifty milligrams of radium properly screened will abolish menstruation for a period extending from three months to a year, or produce a permanent menopause if desired, depending on the number of milligram hours received by the patient. In menorrhagia and metrorrhagia occurring in women near the menopausal age radium is the treatment of choice, but in younger women it should be used with caution. It is ideal for use in non-malignant bleeding of unknown origin, and has given favorable results in controlling endometritis and leucorrhea.

The results with fibroid tumors are uniformly good, some claiming from 90 to 100 per cent of cures without any mortality. If the case is complicated by lateral inflammation dermoid or ovarian cyst, or urgent pressure symptoms, surgical intervention is advisable, and abdominal myomectomy is preferable to radium in cases of definite fibroids with bleeding if the patient is under thirty-five and desirous of having children. Radium acts by producing an endarteritis and also by cauterizing the endometrium of the uterus. It is preferable to the x-ray which causes a cessation of ovarian activity and must be applied a number of times, whereas one application of radium is usually sufficient.

In malignant cancer of the uterus radium is indicated in all operable conditions where constitutional peculiarities make the employment of surgery inadvisable or impossible, and should be used in all inoperable cases or those of recurrence after operation, as it arrests hemorrhage, lessens discharge and retards growth, while ameliorating the pain, healing ulcerations and improving the general condition of the patient. This is true whether the growth occurs in the body of the uterus or the cervix, though the first should be operated if possible and subsequently treated by radium.

Janeway believes radium alone to be the best treatment for carcinoma of the cervix. He compares the results of the Wertheim operation, which in the hands of the best operators gives a mortality of over 25 per cent with the ultimate cure of only 27 per cent, with radium treatment, which has no primary mortality and a far higher percentage of cures. Following operation the three-fourths of the uncured cases are subject to operative sequelae such as vesico-vaginal or recto-vaginal fistula and if the disease has already progressed into the parametrium (as shown by microscopic examination of a uterus removed by Wertheim operation) recurrence and death are inevitable.

In cancer of the breast surgery is advisable, making use of radium if the condition is inoperable or recurs. Radium is very powerful as a prophylactic treatment following operation upon the breast and also after removal of a cervical or uterine cancer. Radium application is particularly useful upon the glands of the axilla.

The growths in the rectum which give the most favorable results after radium treatment are the annular, vascular type, the hard nodular varieties being less amenable to this form of therapy. Radium, however, should be tried in all operable cases. One of my own patients had a carcinoma about seven inches from the anus, which was rapidly closing off the rectum. By radium application I was able to restore the lumen so as to permit the passage of feces. This patient was later prevailed upon to undergo a colostomy and died in two days. In another case where the patient was a woman of 42, there was a growth one inch from the anus which had been present about four months, accompanied by the characteristic symptoms of pain, bleeding, loss of weight, etc. With three radium treatments I not only controlled the symptoms, but also after the lapse of one year the patient appears perfectly cured. This case might have been operated, but by the advice of a very competent surgeon, radium was employed instead.

Carcinoma of the bladder and prostate usually do best under a combination of surgery and radium and if taken early the prognosis is favorable. Radium alone has proved beneficial in these conditions. No cures have been reported in carcinoma of the stomach and intestines, although bleeding has been arrested. In these cases the radium tube is swallowed by the patient and its position in the stomach determined by x-ray.

In carcinoma of the oesophagus the outlook is favorable if the case is seen in the beginning, but this condition in the tongue, palate, or buccal and pharyngeal mucous membranes is very refractory to radium. Better results can be obtained in carcinoma of the tonsil, but in the larynx, although it is advisable to employ radium, the prognosis is very poor. In all mouth cases, any glandular involvement should be surgically treated. Carcinoma of the lip when treated early gives uniformly good results. The cervical glands should either be removed by surgery or treated by deep radium therapy. Here radium has yielded a higher percentage of cures than any other known method.

Sarcoma affecting the naso-pharyngeal region and the lympho-sarcoma at first respond readily to radium treatment, but the improvement is only temporary. The periosteal do better than the endosteal, and the spindle-celled than the round-celled variety. Fibromata of the nose and papilloma of the vocal cords or of the bladder are improved by the employment of radium and some cures have been reported.

Endothelioma—most frequently encountered as a tumor of the parotid gland—does well with prolonged radiation and heavy screening. My case of endothelioma of the right parotid is still apparently well after the lapse of more than a year. Three treatments of 600 mg. hours each were employed. The enlarged thymus glands of children improve greatly with radium treatment. Brayton and Hueblin report the cure of symptoms in thirty-four cases.

In exophthalmic goiter the use of radium in conjunction with routine medical treatment should be strongly advocated. Usually the size of the thyroid is decreased together with a striking symptomatic improvement. The rays reduce the vascularity of the gland by affecting the blood vessels and this diminishing the secretion.

Cancer of the skin may be divided into two classes, the basal-celled or rodent ulcer and the prickle-celled type. I have treated about fifty cases of the basal-celled variety of epithelioma of the face, neck, ears and scalp by means of radium during the past year and the results have been uniformly favorable, both from a curative and cosmetic point of view. I regard radium as the ideal treatment for epithelioma of the eyelids. The cosmetic result is at times almost unbelievably good.

My results with the prickle-celled carcinoma of the face forehead, mouth and tongue have not been so gratifying and I attribute this to the following facts: We are dealing with a very malignant growth, prone to metastases and whatever the method used, if it is to be cured, it must be treated early. All my unfavorable results were in cases either long-standing or where previous treatment had been unsuccessful; some with marked glandular involvement were hopeless from the start. It is often difficult to differentiate between the basal and prickle-celled varieties, especially in the beginning, but if both physician and patient could be brought to realize the importance of instituting proper treatment immediately upon the appearance of a suspicious nodule, we could cure all cutaneous cancers, since radium seldom fails if only it is applied in time.

Many heretofore stubborn and incurable dermatological conditions are now being improved and eradicated by means of radium. It is especially valuable in the angioma of children, because it is painless and easy to apply. Its cosmetic results are superior to those obtained by any other method. Lymphangioma as a rule respond to radium therapy, as do keloids and lupus erythematosus and chronic eczema of the mucous membrane of the lips of which I have been able to cure four cases of lupus erythematosus and two of the mucous eczema. Both lupus vulgaris and erythematosus are distinctly improved by radium therapy and some cures have been reported; tuberculosis verrucosus cutis also responds beautifully to radium, as I discovered in an unusual case in which the nose and cheek were affected.

When plantar warts do not respond to CO₂ snow or the electric needle radium may be of service. A patient of mine, who was a stenographer, was greatly hindered in her occupation by a wart under the nail of the left index finger which had resisted all the usual forms of treatment. Radium affected a complete cure.

In sycosis vulgaris, intractable pururitis (as of the anus) localized eczema and psoriasis, lichenifications, leucoplakia of the first degree, and other skin affections, including x-ray burns, radium is proving invaluable to the dermatologist.

Aiken who has treated one hundred cases of goiter with radium says that its action is about the same as that of the x-ray, but has the advantage of the constant emission of the rays which makes exact dosage possible, of being easily applied without the necessity of a noisy exciting apparatus and of much deeper penetration of the tissue.

Other conditions in which radium is proving extremely useful are tuberculous adenitis, in which—when properly eradicated—the glands become quite small and the disease is arrested by an encapsulating fibrosis; eye conditions such as cataract, conjunctivitis and catarrhal folliculitis; vernal or spring catarrh, in two cases of which I have had remarkable improvement and certain systematic diseases, such as splenomedullary, leukemia, pernicious anemia and Hodgkin's disease, where the therapy has proved beneficial.

During the past year one hundred and fifty-six cases have been referred to me for radium treatment. These included a large variety of epitheliomas, carcinoma, both operable and inoperable, prophylactic treatment following hysterectomy and other surgical interventions, sarcomas of both glands and bones, numerous tubercular conditions and a large number of skin conditions, such as naevi, lupus erythematosus of the lip, lymphangioma of the scalp, etc. The general results have been strikingly favorable.

CONCLUSIONS:

Radium is the ideal treatment for all forms of basal-celled epitheliomas and for prickle-celled epithelioma, if it is seen early and no glandular involvement is present.

Radium is to be preferred in certain uncomplicated cases of uterine fibroid and bleeding and should be universally used in cancer of the cervix and inoperable cancer of the body of the uterus. It is also indicated when carcinoma occurs in other parts of the body when treatment can be instituted early, particularly in the lip, rectum, etc. In all forms of inoperable cancer, it will relieve pain and hemorrhage and lessen discharges.

Radium is of service in the treatment of exophthalmic goitre, certain systematic diseases and various skin affections.

In closing, let me once more endeavor to impress upon the minds of everyone present the great importance of recognizing and treating all forms of cancer at the earliest possible stage, and of curing all pre-cancerous conditions, of the skin, cervix and so on before they have opportunity to become cancerous, by the use of radium or some other reliable agent. From my own experience I feel justified in affirming that radium is here to stay, and that the physician who is not willing to recognize its value to medical science is simply refusing to read the handwriting upon the wall.

4 West Seventh Street.



COMPLIMENTS
OF THE AUTHOR

AN EFFICIENT METHOD OF APPLYING
RADIUM WITHIN THE MOUTH

E. WOOD RUGGLES, A.M., M.D.

ROCHESTER, N. Y.

The treatment of lesions within the mouth with roentgen rays or radium has always been a procedure of the utmost difficulty. It is much more practicable with radium, but the holding of an applicator on one area for hours is intensely wearisome to the nurse, or to the patient if he does it himself. Besides this, it is practically impossible to hold the radium in exactly the same position for any length of time.

Five months ago a Polish girl, aged 6 years, was brought to me for the treatment of an extensive cavernous nevus of the internal surface of the right cheek and the lower lip.

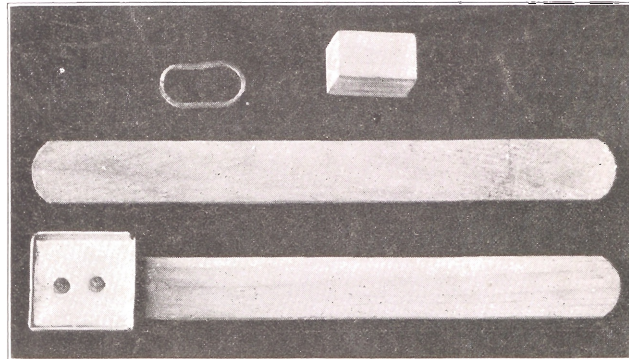


Fig. 1.—Separate parts of apparatus for applying radium within the mouth.

It encroached on the true skin beyond the vermillion border for an area of only about one-quarter by one-sixteenth inch (6 by 1.5 mm.) at the center of the lower lip. The cheek was nearly an inch in diameter at the most prominent part, and the lower lip hung down on the chin, causing a revolting appearance, like an exaggeration of the condition of the lower lip in a full-blooded African negro.

Treatment for this condition meant hours of exposure, and for a moment I was staggered, as the child was too young to hold the radium, and the parents too poor to pay for a nurse and not intelligent enough to do it themselves. It

then occurred to me to attach the radium plaque to the end of an ordinary white pine tongue depressor, which is quite flexible, with rubber adhesive plaster, to locate it properly and then to place a similar depressor exactly opposite on the outside of the mouth. I then placed a rubber band, folded two or three times so as to give adequate pressure, at the center of the depressors, and inserted a block of wood about one-half inch thick between the outer ends.

The pressure produces no pain or even inconvenience except that of leaving the mouth open, even when left in



Fig. 2.—Apparatus in place.

position, as in this case, for five hours (with 0.2 mm. of brass protection). The plaque remains indefinitely in exactly the same location, as can be demonstrated by moving the outer ends up or down. On being released, they return to their original position. In treating the lower lip a cord was attached to the outer ends and looped over the back of the head so as to avoid downward tension on the lip.

The results in this case, while slow, have been very gratifying. The thickness of the cheek has been considerably reduced, and the child is able almost to close the lower lip to its normal position. Some discoloration has appeared near the angle of the mouth, evidently an extension of the nevus

toward the skin, and an indication that, without treatment, the skin over the whole nevus would be involved. This area has not yet been treated, as the other parts were much thicker.

In the same manner I have also treated with radium a precancerous scaly lesion of the vermilion border of the lower lip, which had existed over a year, and the result was perfect. Lesions of the projecting part of the tongue can be treated similarly by increasing the thickness of the block which separates the outer extremities. The same method can be employed with lesions of the skin on the cheeks, lips and ears, especially when greater pressure is desired than can be obtained by adhesive plaster.

Of course the principal condition in which this apparatus would be useful is leukoplakia, but there are several other diseases of the oral cavity in which treatment with radium is indicated; for example, lupus vulgaris and erythematous, epithelioma, carcinoma, lichen planus and, rarely, sarcoma and acanthosis nigricans.

I have endeavored to have the instrument constructed of aluminum, there being an alloy which has considerable flexibility; but I have found that, to secure sufficient springiness, the pieces would be too heavy for comfort and might sag downward. The Standard Chemical Company of Pittsburgh has constructed, at my suggestion, an applicator which, while utilizing the tensile strength of wood, renders it much easier to retain the radium in position. An aluminum box which fits the 2 c.c. radium plaques, and is slightly shallower, is attached to the end of one of the tongue depressors, as shown in Figure 1. At one corner a slot is left, extending to the bottom of the box, so that a small instrument, such as a nail, can be used to dislodge the plaque if it is not easily removable.

I fully believe that this applicator will find wide use if once tested, as it renders the treatment of intra-oral lesions a procedure of the greatest ease and simplicity.

348 University Avenue.

*Reprinted from The Journal of the American Medical Association
May 12, 1923, Vol. 80, pp. 1374 and 1375*

*Copyright, 1923
American Medical Association, 535 N. Dearborn St., Chicago*

*Reprinted from The Journal of the American Medical Association
November 19, 1938, Vol. 111, pp. 1902-1906*

Copyright, 1938, by American Medical Association

RADIOSENSITIVITY OF MALIGNANT NEOPLASMS OF THE UTERINE CERVIX

HARRY H. BOWING, M.D.

AND

ROBERT E. FRICKE, M.D.

ROCHESTER, MINN.

Carcinoma of the uterine cervix is radiosensitive. Radiosensitivity means sensitive to radiant energy; specifically it is used to describe certain tumors that are susceptible of being injured or destroyed by radium and roentgen rays. This fact was soon learned by the early workers in the field of radium therapeutics. The disease was among the first malignant tumors observed to be amenable to the rays of radium.

The radiosensitivity of the lesion under consideration is relative, since the degree of injurability or destroyability is dependent on many factors. Apparently some of these factors can be evaluated, at least in a measure or in a limited degree. Ewing said: "The general condition of the patient determines the result of radiation, regardless of nearly all other factors. In fresh subjects in good general health, without anemia or cachexia, the results of radiation are usually prompt and definite, whereas in anemic and cachectic subjects with poor circulation, tumors may fail entirely to respond." Some of these factors can be recognized grossly while others are recognized microscopically. The former lend themselves rather well to recognition and discussion while the latter may be studied only by examination of material which is removed at operation or for biopsy, and by postmortem examination of specimens by skilled pathologists. As a rule, the supply of tissue for microscopic study is very limited, especially when one considers that the response to

From the Section on Therapeutic Radiology, the Mayo Clinic.
Read before the Section on Radiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

treatment requires days or weeks and that repeated removal of tissue is necessary. During a course of treatment the removal of representative tissue from time to time for microscopic study and for the evaluation of the results of treatment is considered dangerous or inadvisable.

The capacity of a given malignant lesion of the cervix to respond to irradiation can be determined by frequent observations during the course of treatment, and the duration of this response can be in a measure determined by the number of three year or five year cures in a group of cases. The data presented in this paper were obtained from our daily experience and from the three year results obtained in a group of 1,491 cases in which treatment was given in the years 1915 to 1929 inclusive. As a rule the diagnosis can be made from the chief complaint, history, bimanual pelvic examination and inspection of the vaginal cavity, preferably with the patient in the knee-chest position. The removal of small bits of tissue for microscopic study is of value in confirming the clinical diagnosis and in determining the grade of malignancy. Material for biopsy can be obtained with but little, if any, risk. The diagnosis was confirmed by histologic examination in 947 cases; 872 of the 947 patients were traced after they left the clinic; 372, or 42.7 per cent of these patients, lived three or more years after the treatment. In the entire series of 1,371 traced patients 473, or 34.5 per cent, lived three or more years after the treatment. In the early years covered by this study a biopsy was an elective procedure, but at the present time it is performed as a matter of routine. The routine performance of biopsy has advanced our knowledge of this dreaded disease. Malignant neoplasms of the uterine cervix consist chiefly of squamous cell epitheliomas, which have a dominant tendency toward the higher grades of malignancy. The remaining small group is made up of adenocarcinomas and a few mixed lesions which contain both of these malignant cellular elements. In the majority of the cases an extensive primary lesion is associated with an inflammatory or degenerative process and the therapeutic management¹ requires special consideration.

1. Bowing, H. H., and Fricke, R. E.: Carcinoma of the Uterine Cervix: A Survey of Treatment and Results in 1,491 Cases, *Am. J. Roentgenol.* **40**: 47-51 (July) 1938.

From the standpoint of radium therapy it is important to classify the lesions according to the extent of the primary and secondary involvement. The following classification has proved satisfactory: Stage 1 indicates that the primary lesion is limited to the uterine cervix, stage 2 indicates that the primary lesion has extended beyond the original site but the uterus is movable, stage 3 indicates that the primary lesion has extended further than in stage 2 and that the uterus is definitely fixed, stage 4 indicates a "frozen pelvis" with extensive pelvic involvement and the probable presence of local and distant metastasis. The term "modified" is used to describe the stage of involvement in cases in which some type of therapeutic procedure had been employed before the patients came to the Section on Radium Therapy. Modified stage 1 denotes that the active lesion is rather small, while modified stage 4 denotes that a "frozen pelvis" is present.

The radium technic employed at the clinic in the treatment of carcinoma of the uterine cervix may be defined as an intensive, multiple or broken-dose method. This procedure is orderly, flexible and effective. The radium therapist should have at his disposal an assortment of applicators such as universal tubes, various needles and gold (radon) seeds. The treatment factors, that is, the amount of radium, the filtration and the distance, as a rule should remain constant, while the time of application and the interval between applications should be varied to meet the needs of the patient. Nearly all patients are placed in the knee-chest position in order to permit careful inspection and the introduction of applicators without trauma (fig. 1). The intervals are necessary to determine the radiosensitivity of the treated lesion. In cases in which such complications as tumor necrosis, local cellulitis, ulceration of the vaginal walls that is indicative of potential fistulas, or pyometritis are present the intervals permit the proper institution of active measures to combat these serious, if not dangerous, conditions. In the final part of the course, the treatments are applied more rapidly. The other details are shown in figure 2, in which the probable treatment schedule for an average patient with a stage 3 involvement is outlined. The radium therapy is followed by a course

of so-called high voltage roentgen therapy. The combined method of treatment was employed in 1,450 of the 1,491 cases in this series. In the remaining forty-one cases roentgen therapy was the only treatment used.

The classification of the courses of radium treatment is essential for their evaluation. In the event that the

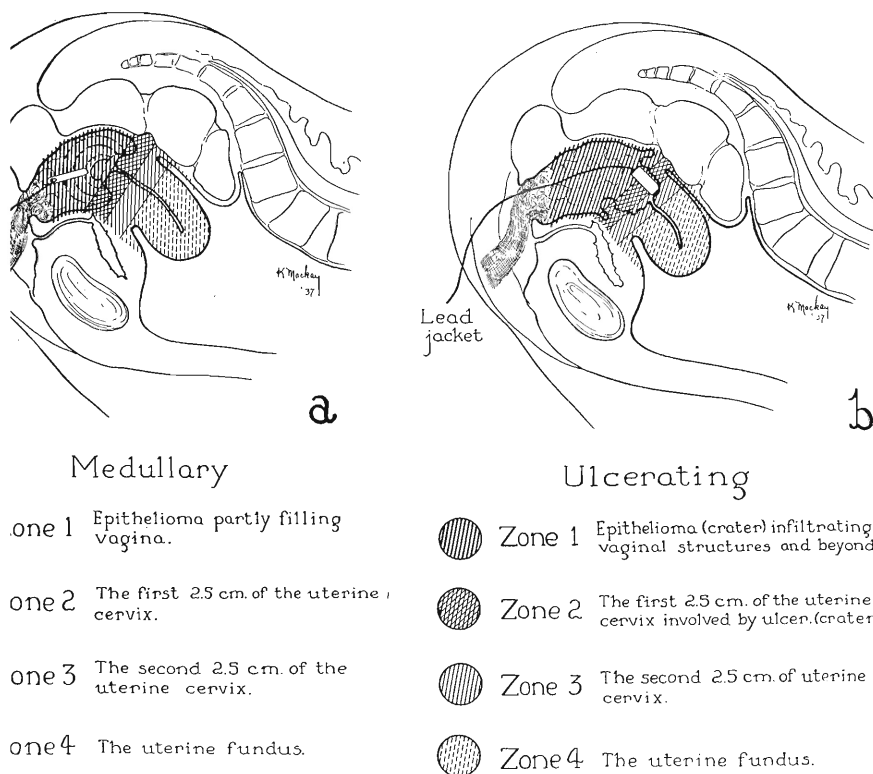


Fig. 1.—Treatment of (a) medullary type, and (b) infiltrating types of uterine carcinoma. Patient in knee-chest position and applicator in place.

treatment is applied as outlined, together with any additional or probable reduction in the number of applicators, it is classed as complete. In some cases, owing to the character and extent of the local or pelvic involvement, only part of the outline can be carried out. In such cases the treatments are classed as limited. During the course of treatment it may become necessary

to stop treatment and in this event the treatment is classed as abandoned. Table 1 shows the most significant factor in estimating the longevity of these patients; 52.9 per cent of the patients who received a complete treatment and 21.4 per cent of those who received only a limited treatment lived three or more years after

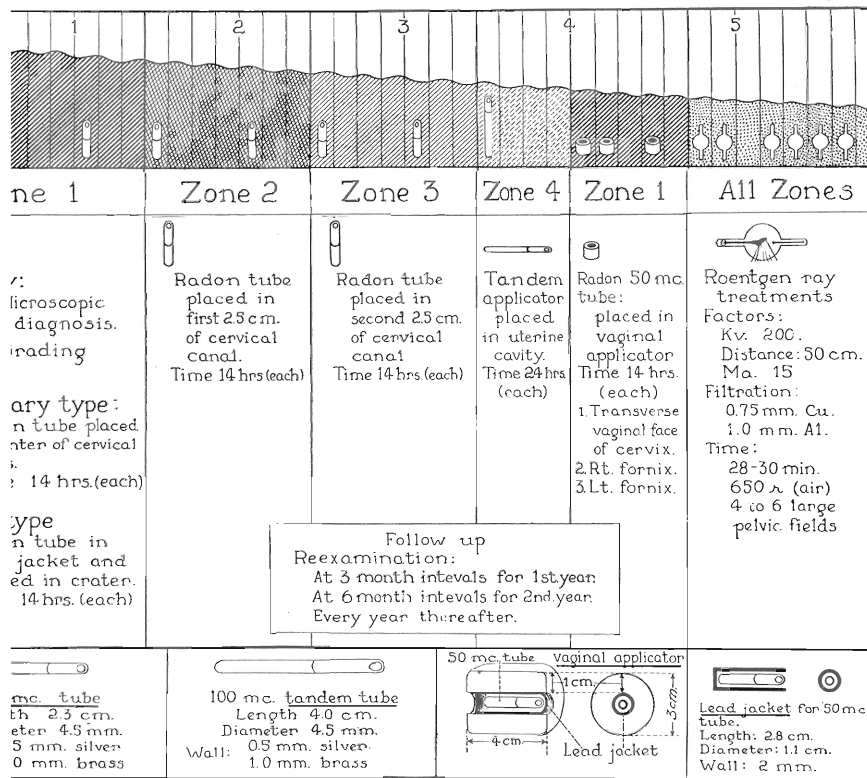


Fig. 2.—Schedule of radium treatment for the average stage 3 involvement in a case of carcinoma of the uterine cervix. Each of the Arabic numerals across the top of the drawing indicates the end of one week of treatment. The vertical line which is intercepted by each Arabic numeral, and every other similar vertical line, indicates the end of one day. The wavy line which descends from left to right indicates the decreasing infiltration and the general improvement of the patient's condition as treatment progresses. Directions for a complete treatment can be obtained by reading the chart from left to right.

treatment. This result is all the more significant because in more than 90 per cent of the 1,491 cases the involvement was extensive (stages 3 and 4, table 2). The

large number of patients who received limited treatments can be explained as follows. They were treated in the early years covered by this study and when compared with the patients treated in the later years of this study their therapeutic management was considered to be a limited treatment. Of the patients

TABLE 1.—*Results According to the Type of Radium Treatment Employed*

Classification of Radium Treatment	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Complete.....	604	565	299	52.9
Limited.....	807	739	158	21.4
Abandoned.....	39	33	10	30.3
Total.....	1,450*	1,337	467	34.9

* This does not include forty-one cases in which roentgen therapy was used alone.

TABLE 2.—*Results of Treatment of Carcinoma of the Uterine Cervix with Irradiation Alone, Based on Stage of Lesion*

Stage of Lesion	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Stage 1.....	13	13	12	92.3
Stage 2.....	85	81	57	70.4
Stage 3.....	825	760	292	38.4
Stage 4.....	156	142	18	12.7
Modified stage 1.....	4	4	4	100.0
Modified stage 2.....	28	26	18	69.2
Modified stage 3.....	297	271	68	25.1
Modified stage 4.....	83	74	4	5.4
Total.....	1,491	1,371 (91.9%)	473	34.5

whose treatment was abandoned 30.3 per cent lived three years or more after the treatment (table 1). Much depends on the amount of treatment applied before it is necessary to stop the applications. The analysis of this group is fascinating; many of the patients who lived three or more years after the treatment received a very limited treatment. The associated complications may have been a deciding factor in the response to radium therapy.

We have no statistical data to confirm the statements made about the immediate or initial result. However, the patients who lived three or more years after the treatment may furnish an index. All treatable patients are benefited. The vaginal discharge stops, the tendency to bleed stops, and in many cases the relief of pain is prompt. The degree and the duration of this improvement depend on the extent of malignant involvement and the adequacy with which treatment can be applied.

The patient with stage 1 and modified stage 1 involvement has the best chance of living three or more years after treatment; while the patient who has stage 4 and modified stage 4 involvement has the least chance of living three or more years after treatment. In brief, all treatable patients have a chance of living three or more years after treatment (table 2). An evaluation of these results indicates that the extent of involvement plays a major role in the determination of the longevity of the patient after treatment.

Grossly, there are two types of carcinoma of the uterine cervix; these usually are designated as (1) medullary carcinoma and (2) infiltrating or ulcerating carcinoma. The latter type predominates and is more radioresistant than is the former. The grade of malignancy cannot be determined from the gross characteristics of the lesion. However, the gross appearance of the lesion does determine the selection of the type of treatment to be employed in a given case. In other words, the estimation of the grade of malignancy is of but little if any assistance to the radium therapist in determining the treatment to be employed. This statement must be made with a certain amount of reservation because a low grade of malignancy seldom is encountered in cases of carcinoma of the uterine cervix and when it is encountered the neoplasm usually is an adenocarcinoma. It is doubtful whether a squamous cell epithelioma, grade 1, was ever encountered.² In other words, our experience centers around the predominating grade 3 and grade 4 lesions. It is evident that if a number of patients who have carcinoma of the cervix are treated individually, irrespective of the grade of malignancy, and if the patients later are grouped according to the grade of malignancy, there

2. Broders, A. C.: Personal communication to the authors.

will be little difference in the number of three year cures obtained in the various groups. The data in table 3 are submitted to substantiate this statement. Forty per cent of the patients with lesions of grade 1 and 41.1 per cent with lesions of grade 4 lived three or more years after treatment.

Briefly, it seems possible to obtain the same radiotherapeutic result in the treatment of this disease regardless of the grade of malignancy, but one must remember that the cases in which the grade of malignancy was low were very few in number and do not warrant a statistical review or opinion. These statisti-

TABLE 3.—*Results of Treatment of Carcinoma of the Uterine Cervix with Radiation Therapy, Based on the Grade of Malignant Change*

Grade of Malignancy	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Grade 1.....	5	5	2	20.0
Grade 2.....	135	125	56	44.8
Grade 3.....	407	372	161	43.3
Grade 4.....	336	311	128	41.1
Biopsy performed but malignancy was not graded.....	64	59	25	42.4
No biopsy performed..	544	499	101	20.2
Total.....	1,491	1,371 (91.9%)	473	34.5

cal data warrant further study. We are in accord with MacCarty's statement that one is prone to accept observations too quickly and is likely to draw premature conclusions; this especially is true of microscopic grading and sensitivity.³

In order to study the influence of age on the longevity of this group of patients they were grouped according to their ages by decades (table 4). It is an accepted fact that young patients do not tolerate malignant disease as well as do older patients. In other words, the young patient with malignant disease has a poorer prognosis than does an older patient. The data in table 4 substantiate this statement. The number of

3. MacCarty, W. C.: Microscopic Grading of Tumors, Its Interpretation, Limitations and Relation to Radiosensitivity, *Am. J. Roentgenol.* **37**: 365-367 (March) 1937.

three year cures of patients treated before the age of 49 years was less than it was of patients treated after the age of 49 years. Patients who were in the fourth and fifth decades of life when radiation therapy was started showed little difference in the percentage of three year cures; however, this statement does not hold true if the patients who were in the third decade of life are included. This may indicate that if it is possible to employ individual treatment for patients in the fourth and fifth decades of life the percentage of three year cures will be approximately the same in the two groups. The percentage of three year cures

TABLE 4.—*Results Obtained in the Treatment of Carcinoma of the Uterine Cervix with Irradiation, Based on Age of Patients*

Age of Patient, Years	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
20 to 29.....	28	25	5	20.0
30 to 39.....	284	266	78	29.3
40 to 49.....	496	458	145	31.6
50 to 59.....	452	416	160	38.5
60 to 69.....	208	185	78	42.2
70 to 79.....	22	20	6	30.0
80 to 89.....	1	1	1	100.0
Total.....	1,491	1,371 (91.9%)	473	34.5

was increased for patients who were beyond the age of 49 years. It seems probable that age may influence the degree of radiosensitivity but it is possible that the primary lesion responds equally regardless of the age of the patient. However, if metastasis to distant organs occurs before the age of 49 years it may be the factor that reduces the number of three year cures. We do not have data that confirm or disprove this statement.

A second significant factor occurs in the data contained in table 5. The patients treated early in our experience received a limited radium treatment, for example about 2,000 mg. hours, which may be considered a surface treatment. This was supplemented with the so-called low voltage roentgen therapy and the initial result was favorable; when the patients were

seen after an interval of a few weeks, or months, however, activity was demonstrable. As a further palliative procedure the initial treatment was repeated. Many patients received several such treatments but, as a rule, malignant activity was demonstrated on subsequent visits. A careful review of these cases was encouraging but it was evident that the technic was deficient as it did not provide proper distribution of the therapeutic rays of radium, and the initial total dose was too small. For these reasons our present technic was evolved; this accounts in a great measure for the difference in results shown in table 5. Today an initial complete treatment is never repeated and the result is superior

TABLE 5.—*Results of Radiation Therapy According to Five Year Periods in Which Treatment Was Given*

Five Year Period in Which Treatment Was Given	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
1915 to 1919, inclusive..	288	264	38	14.4
1920 to 1924, inclusive..	556	522	185	35.4
1925 to 1929, inclusive..	647	585	250	42.7
Total.....	1,491	1,371 (91.9%)	473	34.5

when compared with our early results. Of the patients treated between 1915 and 1919 inclusive 14.4 per cent and of the ones treated between 1925 and 1929 inclusive 42.7 per cent lived three or more years after treatment. The radium technic employed today began to take form in or about the year 1920. We were favorably impressed with the early results, which encouraged us to persevere and perfect our present plan of treatment.

The hospital mortality was calculated on the basis of the type of treatment applied (table 6). There were 604 complete treatments with one death, a mortality of 0.2 per cent. There were 807 limited treatments with five deaths, a mortality of 0.6 per cent. Every endeavor is made at the time the patient is first seen to select the best type of treatment to meet the therapeutic needs. In other words, every effort is

made to avoid, if possible, abandoning treatments. When one considers the numerous applications made throughout the years, the risk attached to a single treatment must be very small; however, the cumulative effect cannot be ruled out. A limited treatment indicates an extensive pelvic involvement and poor general health; it naturally indicates that the risk of treatment would be increased. The hospital mortality in the cases in which the treatment was abandoned was 15.4 per cent. The hospital mortality in the entire series was 0.8 per cent.

TABLE 6.—*Hospital Mortality Based on the Classification of Radium Treatment Applied*

Type of Treatment	Patients	Hospital Deaths	
		Number	Per Cent of Those Who Were Traced
Radium:			
Complete.....	604	1	0.2
Limited.....	807	5	0.6
Abandoned.....	39	6	15.4
Roentgen therapy alone*.....	41	0	
Total.....	1,491	12	0.8

* Included in table to account for full total of cases. Not accepted for radium treatment.

SUMMARY

The radiosensitivity of carcinoma of the uterine cervix is a relative feature and its significance must be fully appreciated in the therapeutic management of this disease. If carcinoma of the uterine cervix and the associated inflammatory and degenerative process are effectively treated with radium and supportive measures, the result of treatment is prompt and its duration is evidenced by the percentage of three year cures. An attempt has been made to use the late results as an index of the radiosensitivity of the lesion. Patients possess many potentialities which affect the results of irradiation. The immediate result is influenced definitely by the extent of the malignant process. It is evident that the age and general health of the patient, the equipment and the skill and experience of the therapeutic radiologist have a definite influence on the late result. The best results are obtained in cases in which

the treatment is classed as complete at the first session. However, subsequent treatment may produce relief that will last for years. The initial course of radium treatment requiring two, three or more weeks is necessary before one can evaluate the immediate results and determine the radiosensitivity of the lesion. An interval of three months should elapse before one attempts to evaluate the late results. We fully appreciate the limitations of statistical data; however, the data in this paper are supported by our clinical experience.

INSTITUT DU RADIUM DE L'UNIVERSITE DE MONTREAL
ET DE LA PROVINCE DE QUEBEC

Le Traitement d'un cancer de la verge par la curiethérapie

Exérèse de Ganglions Métastasiques
Guérison apparente depuis trois ans

*Par le Docteur J.-E. GENDREAU,
Directeur de l'Institut du Radium.*



MONTREAL

1927

Extrait de l'Union Médicale du Canada, décembre 1927.

LE TRAITEMENT D'UN CANCER DE LA VERGE PAR LA CURIETHÉRAPIE

EXÉRÈSE DES GANGLIONS MÉTASTASIQUE

GUÉRISON APPARENTE DEPUIS TROIS ANS

Par le Docteur J.-E. GENDREAU

Les chirurgiens de l'American College of Surgeons et les Radiologistes de l'American Roentgen Ray Society qui ont assisté aux cliniques de l'Institut du Radium de Montréal durant leur dernier congrès, ont particulièrement remarqué et examiné un cas de cancer avancé du pénis guéri depuis trois ans.

La guérison est remarquable parce que le pénis a été conservé entier avec ses fonctions, grâce à un traitement curithérapique très électif, à distance, avec grande filtration.

Il n'y a pas encore, à ma connaissance, de publication signalant en France plusieurs résultats semblables dans les cas avancés avec métastase.

Jean Ricaud vient de faire une revue de la question jusqu'en 1927. Il écrit dans sa thèse de la Faculté de Médecine de Paris, que le traitement de choix est l'amputation de la verge, suivi six semaines après de l'exérèse ganglionnaire; les rayons X ne donnent pas de bons résultats, le radium pourrait dans les cas au début faire espérer la guérison sans mutilation."

Au congrès de l'Association française pour l'avancement des sciences tenu récemment en 1927, deux cas de cancer de la verge traités par la curiethérapie ont été rapportés en Algérie. Dans le premier cas l'adénite inguinale, qui a spontanément disparu, n'était qu'inflammatoire; dans le second, elle a cédé à la Roentgenthérapie, mais il n'y avait pas eu d'examen histologique des ganglions.

Les auteurs ont employé la Radiumpuncture, avec des aiguilles à filtration relativement faible (0.5 mm. de platine). Ils ont rencontré des complications: radiumdermite, induration, sclérose accentuée du gland, rétrécissement serré indilatable, — ennuis qui ont exigé l'intervention du chirurgien dans les deux ans.

En somme, les radiations utilisées semblent encore trop caustiques, et parce que la filtration est réduite à 0.5 mm. de platine, et

surtout parce que l'interaction des aiguilles produit un rayonnement secondaire diffusément destructeur.

Au Tonkin, A. Le Roy des Barres et P. Heyman ont aussi traité plusieurs cancers de la verge, étendus et profonds, mais sans métastases ganglionnaires histologiquement constatées. Ils ont utilisé la même radiumpuncture avec des doses moindres, 15 à 20 millicuries détruits au lieu de 50, et ils ont eu conséquence moins de complications.

Aux Etats-Unis, dans l'*American Journal of Roentgenology*, jan. 1926, A. L. Dean a rapporté 62 cas de cancer du pénis traités par la radiothérapie et la chirurgie au Memorial Hospital de New-York. Il condamne l'introduction des tubes radioactifs dans la tumeur, (méthode des "bare tubes"), et il fait des applications externes, peu filtrées (0.5 mm. d'argent), en contact presque immédiat avec la verge.

Dans les cas avancés, que nous avons en vue, il a toujours pratiqué *l'amputation de la verge*, parce que la méthode conservatrice lui a paru insuffisante. "When the growth extends to the deeper parts of the penis, amputation after irradiation appears to be necessary. This situation exists even though our endeavor has been to devise a type of radiation which unaided will effect a cure." Il est donc opportun d'attirer l'attention sur l'un de ces cas avancés avec métastases où la verge a été conservée, et sur la technique utilisée dans la guérison.

Dossier 413 de l'Institut du Radium de Montréal

Epithélioma mixte, spino-baso cellulaire du pénis avec métastases ganglionnaires dans les deux aines.

Depuis janvier 1924 le malade urine difficilement. Prurit.

En juillet 1924 il est opéré pour un phimosis congénital infecté.

En août 1924, apparition sur le gland d'une tumeur qui se développe en bourgeonnant.

Le 9 janvier 1925, à la première consultation radiologique, on constate un épithélioma ulcéré du gland envahissant les corps caverneux avec perte de substance et chou-fleur. Dans le pli de l'aîne, des deux côtés, ganglions mobiles mais durs, ligneux, indolores.

Examen histologique

1° De la tumeur primitive. "Epithélioma pavimenteux avec globes épidermiques."

2° Des ganglions cancéreux, fait à deux reprises. "Métastase évitée d'épithélioma pavimenteux."

Le 10 janvier 1925, exérèse bilatérale des ganglions envahis.

Traitement curiethérapique

Le 19 janvier 1925, le traitement est commencé lorsque tout danger d'infection actuelle a disparu; le facteur *infection* a toujours une grande importance et l'irradiation la mieux ordonnée échoue généralement sur les tissus ou ganglions chargés de pus.

Applicateur très léger, en bois façonné au tour, en mince coupole, 50 millicuries de radon en tubes de plomb de 2 mm. de paroi, filtration secondaire, aluminium, bois et air. Dose totale à l'émission, 100 millicuries détruits en deux jours, dirigée sur le pénis à une distance minima de 4 cm.

Réaction modérée. Œdème sans radiumdermite ni induration persistante. Le malade laisse l'hôpital le 24 janvier 1925. Une fois par semaine, durant quatre mois, il reviendra à l'hôpital pour une dilatation, qui assure, dans l'intervalle des sept jours, des mictions goulûes mais cuisantes au début.

Roentgenthérapie profonde

Durant les six premiers mois qui suivirent la cicatrisation, deux séries de traitement sont données. Entre la première et la seconde, extirpation, sous anesthésie locale, d'un petit ganglion cancéreux, à droite, dans la pointe du triangle de Scarpa.

Dose totale, environ 5000R français sur la surface des territoires ganglionnaires de chaque côté, en 15 séances; champs à la peau 10 cm.2; filtre, cuivre 1 mm., aluminium 1 mm.; distance 50 cm.; tension de 170 à 180 K.V. de 2 à 2½ milliampères; appareillage: Geiffa, Standard, Ropiquet, ampoules Coolidge dans l'air.

Etat actuel. M. V. a été récemment et soigneusement examiné par plusieurs médecins, notamment par les congressistes chirurgiens et radiologistes dont j'ai déjà parlé.

Localement, le membre viril paraît normal et toutes les fonctions s'exercent normalement sauf une légère cuisson qui a toujours existé au début de la miction et de l'éjaculation spermatique. L'état général est très bon et permet un travail régulier.

En somme, cette observation montre les avantages d'une technique utilisant un rayonnement homogène très sélectif, et la nécessité d'une étroite collaboration entre les radiologistes et les chirurgiens.

BIBLIOGRAPHIE

- Asmus, V.**—Résultats du traitement de l'épithélioma de la verge. Thèse Faculté de Méd., Paris, 1927.
- Astraldi, A.**—Algunas consideraciones sobre el cancer del pene. Bol. Inst. de med. exper para el estud. y trat. del cancer, Buenos Aires, 1924-25, I, 433-437.
- Barringer & Dean.**—Epithelioma of the penis. J. Urol. 1924, XI, 497-514.
- Barringer, P.S., & Dean, S. L.**—Epithelioma of the penis. Radium Report of the Memorial Hospital, New York, Hoeber, 1924.
- Buschke, A., & Lowenstein, L.**—Ueber carcinomahnliche Condylomata acuminata des Penis. Klim. Wchnschr., Berl, 1925, IV, 1726-1728.
- Catef, C.**—Tre casi di epitelioma del pene. Riv. ospedal., Roma, 1925, XV, 513-525.
- Carlisle, J. B.**—Carcinoma of the penis. J. Missouri M. Ass., St. Louis, 1925, XXII, 467-469.
- Chavannaz.**—Epithélioma de la verge. Journal de Méd. de Bordeaux, 25 fév. 1927.
- Chevassu, Maurice.**—Diagnostic du cancer de la verge. Presse Médicale, Paris, 18 septembre 1926.
- Darbresse-Morelle, E.**—Cancer du pénis avec larges métastases inguinales traité par le radium: résultats immédiats; stérilisation apparente se maintient depuis huit mois. Ann. de l'Inst. chir. de Brux., 1926, XXVII, 30-33.
- Dean, Archie L.**—The treatment of the epithelioma of the penis with radium and Roentgen Rays. Amer. Jour. of Roentg., New-York, jan. 1926, 36-43.
- Eyssette-Aucaigne.**—Le traitement du cancer de la verge par la curiethérapie. Thèse Fac. Méd. Alger, 1927.
- Ferrari, F., & Viallet, Ch.**—Le traitement du cancer de la verge par la curiethérapie. Jour. de Radiologie et d'électrol., Paris, sept. 1927.
- Ferrari.**—Cancer de la verge. Curiethérapie. Soc. de Chir. Paris, fév. 1926.
- Foderl, V.**—Zur Klinik und Statistik des Peniskarzinomes. Deutsche Ztschr. f. Chir., Leipz., 1926, CXCVIII, 207-230.
- Gibbs, W. W.**—Epithelioma of the penis. J. Nat. M. Ass., Newark, N.J., 1926, XCIII, 200-202.
- Gilliam, D. B.**—Carcinoma of the penis, with report of two cases. Urol. & Cutan. Rev., St. Louis, 1924, XXVIII, 390-392.
- Jeanneney, G.**—Cancer du penis récidivé. Considérations thérapeutiques. J. de méd. de Bordeaux, 1926, LVI, 693-695.
- Jeanneney, G.**—Cancer du pénis. Le Cancer. Paris, Maloine, 1926, p. 112-115.

- Kelly, H. A., & Ward, G. E.**—The treatment of carcinoma of the penis with endothermy with a method of treatment of metastatic malignant lymph glands. Report of a case. Surg. Gynec. & Obst., Chicago, 1926, XLII, 712.
- Le Jeune.**—Sur quatre cas d'épithéliome de la verge. Arch. de méd. et pharm. nav., Par., 1924, CXIV, 148-153.
- LeRoy des Barres & Heyman.**—Le cancer de la verge au Tonkin. Jour. de Radiol., Paris, fév. 1927.
- Mark, E. G.**—Sarcoma of the penis. J. Urol., Balt., 1926, XV, 611-617.
- Mackenzie, A. J., & Koster, B. McD.**—Endothelioma of the corpus cavernosum penis, a case report. St. Michal's Hosp. Med. Bull., Toronto, 1923-24, I, 39-47, 3 pl.
- McKim, G. F., & Smith, P. G.**—Carcinoma of the penis. Cincinnati J. Med., 1925-26, 193-195.
- Nabias, S. de.**—Traitement par le radium de quelques néoplasmes. Paris, Chahine, 1928.
- Keynes, H.**—A propos des cancers de la verge. Arch. franco-belges de chirurgie, Brux., 1924, XXVII, 926-932.
- Ricaud, Jean.**—Contribution à l'étude du cancer de la verge. Thèse Fac. Méd. Paris, 1927.
- Simpson, F. E.**—Radium Therapy. St. Louis, 1922, p. 208.
- Southern, C. M.**—Cancer del pene; nueva tecnica. Semana méd., Buenos Aires, 1924, XXXI, 735-739.
- Whiteford, C.H.**—Epithelioma of penis following incomplete circumcision. Med. Press, Lond., 1925, n. s., CXIX, 25.
- Wilenki, A. O.**—Carcinoma of the penis. J. Urol., Balt., 1926, XVI, 391-396.

— o —







INSTITUT DU RADIUM DE L'UNIVERSITE DE MONTREAL
ET DE LA PROVINCE DE QUEBEC

Les complications infectieuses de la radiothérapie du col utérin

A propos d'un cas de guérison apparente

Par le Docteur J.-E. GENDREAU,
Directeur de l'Institut du Radium.



MONTREAL

1927

Extrait de l'Union Médicale du Canada, novembre 1927.



LES COMPLICATIONS INFECTIEUSES DE LA RADIOTHÉRAPIE DU COL UTÉRIN

A PROPOS D'UN CAS DE GUÉRISON APPARENTE

Par le Docteur J.-E. Gendreau.

Au congrès de l'American Radium Society à Washington, en mai 1927, j'ai suivi avec un intérêt particulier les travaux sur les complications, immédiates ou tardives, qui résultent de l'usage du radium en Gynécologie.

L'omission de certains détails importants de la technique européenne m'avait frappé, et j'ai saisi l'occasion de les exposer aux membres de l'American Roentgen Ray Society, qui sont venus, lors de leur dernier congrès à Montréal, visiter l'Institut du Radium et examiner les cas de guérisons présentées.

J'ai attiré leur attention spécialement sur une malade guérie en apparence, depuis un an, d'un cancer inopérable du col utérin; elle avait souffert d'une infection secondaire exceptionnellement sérieuse et rebelle.

Une telle complication offre, encore actuellement, l'obstacle peut-être le plus difficile à surmonter, dans la guérison du cancer du col utérin par les radiations; le docteur Claude Regaud le premier en a signalé l'importance.

Les agents infectieux sont quelquefois introduits par des manœuvres utéro-vaginales septiques, et le traumatisme local causé par le traitement curiéthérapique, si modéré qu'il soit, en favorise la diffusion; d'autres fois, et ces cas sont les plus fréquents, l'infection existe dans les tissus avant le traitement, soit qu'elle n'ait pas été combattue au préalable, échappant aux contrôles bactériologique et clinique, soit enfin qu'on ait dû traiter quand même d'urgence, et essayer de sauver la patiente malgré les risques.

Ces risques sont grands, car les applications radiothérapiques doivent être intensives, sinon dans le temps, du moins dans la dose totale. Or ces radiations intensives, qui doivent détruire électivement toutes les cellules cancéreuses, diminuent dans une certaine mesure la résistance à l'infection des tissus normaux, même si elles sont données exclusivement de l'extérieur, comme dans la Roentgen-thérapie et la Curithérapie à distance.

On voit des malades avancés qui ne résistent pas à l'infection, faute de soins spéciaux, qu'un entourage très dévoué ne saurait leur assurer, même dans un hôpital spécialisé. La lutte est souvent longue et pénible et le succès n'est jamais certain dans l'état actuel de la science.

Une guérison dans ces circonstances est toujours instructive et appréciée. Le cas suivant est donc relaté, non pas parce qu'il nous montre la disparition depuis un an de tout symptôme de cancer chez une patiente inopérable et avancée, mais à cause des complications infectieuses rencontrées et vaincues.

Dossier 857 de l'Institut du Radium de Montréal

Madame C..., 33 ans. Ménagère.

Epithélioma du col de l'utérus, forme ulcérée, cavitaire, l'utérus est immobilisé, les paramètres sont envahis, la malade est inopérable (Dr R. Trudeau, Hôpital Notre-Dame). Quatre grossesses et accouchements à terme. Déchirure du périnée au deuxième degré. Entre les époques, hémorrhagie intermittentes, surtout depuis janvier 1926. Ecoulements continus, roussâtres, fétides, polyurie nocturne. Douleurs dans les régions hypogastrique et lombaire se propageant dans les cuisses depuis mai 1926. Insomnie, malgré la morphine, incapacité absolue de travail, teint sub-ictérique, amaigrissement considérable. Poids 95 livres. (Premier examen à l'Hôpital Notre-Dame.)

Rapport histologique

"Prolifération épithéliomateuse atypique envahissant la partie endo-cervicale en s'insinuant entre les tubes glandulaires.

"Mitoses très nombreuses, dégénérescence fibrinoïde du stroma en plusieurs points, ailleurs infiltration lymphoplasmocytaire

"En résumé: Epithélioma atypique du col, qui bénéficiera très peu d'un traitement par les rayons. La dégénérescence fibrinoïde du stroma *contrindique même ce traitement.*"

Malgré ces contrindications histologiques d'un examen fait en dehors de l'Institut du Radium, et pour des motifs que j'exposerai dans travail ultérieur, le traitement curiethérapique fut décidé.

La malade entre à l'Hôpital Notre-Dame le 28 octobre; elle est préparée, désinfectée durant cinq jours; la température dépasse 101.2° le soir. Le 29 au matin le radium est appliqué d'après la technique suivante :

Curiethérapie

Sonde intra-utérine en caoutchouc pur. Deux foyers linéaires de 6.6 milligrammes de radium élément chacun. Filtration primaire de 1.5 millimètre de platine iridié. Colpostat vaginal à trois foyers séparés, de 13.3 milligrammes de radium élément chacun. Filtration primaire de 1.5 millimètre de platine iridié; filtration secondaire de 1 centimètre de liège paraffiné.

Tous les tubes furent laissés en place durant cinq jours et quatre heures, donnant à l'intérieur de l'utérus une dose de 12.5 millicuries détruits et de 36.5 millicuries détruits dans le vagin.

Réaction

Malgré la modération de la dose, la réaction est vive; le soir du 29 octobre, la température atteint 103.3°, redescend à 102° les jours suivants, s'élève encore à 103° le 9 novembre, oscille, passe à 101° le 20 novembre, et de même le 22 novembre lorsqu'elle est transportée à l'Institut du Radium pour y recevoir les traitements de Rayons X complémentaires.

Le 27 novembre, après deux séances de Roentgenthérapie, la température est à 102° et il faut interrompre l'irradiation et traiter spécialement l'infection menaçante.

Malgré tous les désinfectants chimiques, les écoulements vaginaux gris verdâtres deviennent plus abondants, les urines purulentes et fétides; les selles sont rares et les douleurs abdominales augmentent.

Auto-vaccin

Le 6 décembre, nous décidons d'utiliser la vaccination locale; le Docteur Lorenzo Jutras fait les prélèvements et commence la préparation, dans le laboratoire de l'Institut du Radium, d'un auto-vaccin mixte. Le 7 décembre, la température est à 102°. Le 8 décembre, le pouls est à 104, palpitations; on commence l'huile camphrée à 10 cc. par injections quotidiennes. Le 9 décembre, la malade est très faible et se prépare à la mort. Le 10 décembre, le pouls est à 126; première application d'auto-vaccin, sous la forme de pansements vaginaux avec mèche imbibée, renouvelée chaque jour. Les injections sous-cutanées intradermiques d'autovaccin restent sans effet sur les infections streptococciques (Mutermilch et Lavedan). Le 12 décembre, le pouls est à 118, le 13 décembre, la tempé-

rature atteint 102.4° et le 14, 104°. Le 15 décembre, la température est à 103.4°; les écoulements changent d'aspect, ils pâlisent. Le 17 décembre, la température est à 103°, et à 100.4° le 18 décembre. Le 19 décembre, la température est à 99°, le pouls à 92. Du 19 au 24, la température est presque normale, le pus devient plus jaune, donne moins d'odeur. Le 22 décembre, la patiente demande à manger. Le 24 décembre, elle se soulève dans son lit pendant dix minutes, frisson, indigestion, vomissements; le soir, la température est à 102°. Le 25 décembre, la température atteint 105°, le pouls 142, la respiration 32, le facies très pâle. Les pansements à l'auto-vaccin sont répétés deux fois par jour, combinés avec les douches à solution sucrée hypertonique, d'après la méthode de Nogier.

Le 26 décembre, la température est à 104.4°, le 27 à 102°, le 28 à 101.4°. Les écoulements sont moins purulents, les douleurs diminuent. Le 29 décembre, la température est à 99°. Le 31 décembre, la température est normale, l'odeur est moins fétide. Le 4 janvier 1927, encore un peu de pus sur les mèches d'auto-vaccin, qui seront continuées jusqu'à cessation complète de l'écoulement. Le 6 janvier, les urines sont normales; la malade recouvre graduellement des forces.

Roentgenthérapie

Le 20 janvier, la malade est portée à la salle de Roentgenthérapie pour la reprise des irradiations quotidiennes. Le 11 février, dernier prélèvement bactériologique. Le 13 février, la malade a évidemment engraisé. Le 18 février, elle descend seule à la salle de Roentgenthérapie. Le 21 février, première selle sans laxatif. Le 7 mars, les douches reviennent limpides, pour la première fois. Le 12 mars, la malade peut retourner chez elle et faire ensuite chaque jour le trajet pour suivre les traitements de Rayons X.

En somme, depuis son entrée à l'Hôpital du Radium le 22 novembre 1926, la malade avait reçu 55 applications d'auto-vaccin, 86 douches hypertoniques, 360 cc. d'huile camphrée, en 36 injections, 104 doses de strychnine (1/60), 36 frictions à l'alcool, 127 doses toniques et minéralisantes, 56 laxatifs, 43 mixtures digestives.

Technique Roentgenthérapique

Irradiation totale de 25 heures, par 52 séances, sur 43 jours; quatre portes d'entrée de 160 à 250 cent. carrés à la peau, deux

antérieures, deux portérieures; tension moyenne 170 K.V., $2\frac{1}{2}$ milliampères, filtre 2 mm. de zinc et un mil. d'aluminium, distance 50 cm.; dose 9000 R français; coefficient de transmission de 35 à 42%. Appareillage Veifa, Standard, et Gaiffe tension constante, Coolidge dans l'air.

Etat actuel de la malade, un an après le traitement curiethérapique: aspect extérieur de santé presque florissante, la teinte sub-ictérique, la pâleur sont disparues, elle a gagné 25 livres, et pèse 120 livres, pas de douleurs pelviennes, vésicales, rectales, ou crurales; les hémorragies ont cessé, les règles ne sont pas revenues.

A l'intérieur, les ulcérations n'existent plus, le vagin est peu modifié, les infiltrations péri-utérines ont considérablement diminué, les culs-de-sac sont assouplis, l'utérus est plus mobile; la muqueuse saigne encore un peu sous le contact d'un examen très poussé.

Conclusions

Le danger des complications infectieuses impose la ligne de conduite suivante dans le traitement radiothérapique d'un cancer du col utérin :

1° Hospitalisation de la malade avant l'application, pour tous les examens de clinique et de laboratoire, et pour la désinfection par les méthodes appropriées: bactériothérapiques, sérothérapiques, chimiothérapiques, à tonicités diverses, et ionothérapiques (Wintz). Le streptocoque, étant particulièrement résistant, ne cédera probablement qu'à l'auto-vaccin, les badigeonnages et pansements locaux, ou au propidon (Laborde et Wickham).

2° Asepsie chirurgicale dans l'application utéro-vaginale; prudence et surveillance durant le traitement radiothérapique qui ne doit généralement recommencer qu'après l'élimination de tout signe d'infection.

L'intensité horaire de l'irradiation ne doit pas être trop élevée tout en restant suffisante, et efficace.

3° Prolonger l'hospitalisation durant la réaction, soutenir les forces, et donner tous les soins antiseptiques usuels au vagin, rectum et vessie, et combattre les complications par les méthodes déjà indiquées.

Il est évident que cet ensemble si facilement esquissé, mais si difficile à combiner, exige la collaboration de spécialités multiples que

le traitement actuel du cancer réunit autour du même lit; c'est ainsi que nous aurons la grande satisfaction de réaliser quelquefois cette œuvre d'art, de science, de dévouement qu'est la guérison d'un cancer du col utérin inopérable et avancé, et que pour ces cas au moins les plus sceptiques seront forcés de dire avec J. L. Faure (Cancer de l'Utérus, 1925): "Il y a un traitement qui aujourd'hui est cent fois "supérieur à tous les autres, c'est le traitement par le Radium... Je "suis certain qu'il est aujourd'hui démontré que pour les cancers "inopérables, le radium donne des résultats admirables, et qui sont "au-dessus de tout ce que nous aurions pu rêver, il y a une vingtaine "d'années, dans cette triste période où les chirurgiens, découragés, "n'essayaient même pas de soigner les pauvres femmes pour lesquelles "ils avaient perdu tout espoir et les abandonnaient aux consolantes "illusions que donne la morphine."

BIBLIOGRAPHIE

- Bailey et Edith Quimby.**—Sur l'emploi du radium dans le cancer des organes génitaux de la femme. *Journal de Radiologie et d'Electrol.* Paris, Oct. 1922.
- Baud, Mlle.**—Les complications infectieuses de la curiethérapie des cancers de l'utérus. Paris, 1923.
- Bainbridge.**—Le problème du cancer. Paris, 1922.
- Béclère, Cottenot, Mme Laborde.**—Radiologie, Radiumthérapie. Maloine. Paris, 1922.
- Brooks, C. D.**—Radiotherapy in inoperable Carcinoma of the cervix. *The American Journal of Roentgenology*, December 1925.
- Canti, R. G., and Spear, F. G.**—Discussion on pathological basis of treatment by radiation. *Brit. Med. J.*, Aug. 1, 1925.
- Coudamin.**—De la curiethérapie des cancers utérins. *Lyon Médical*, 21 août et 1er sept. 1921.
- Coudamin et Nogier.**—Limites et contrindications de la Radiumthérapie des cancers utérins. *Lyon Médical*, mars 1918.
- Dechambre, S.**—De la Technique de la Curiethérapie par les voies naturelles dans le cancer du col utérin. Paris, Le François, 1923.
- Declairfayt.**—La piogenèse aseptique artificielle auxiliaire de radiations pénétrantes dans la thérapeutique du cancer. *Jour. de Radiologie et d'Elect.*, Paris, sept. 1924.
- Donaldson, M., et Canti, R. G.** (Londres).—Observations sur 50 cas de cancer du col de l'utérus traités par le Radium. *Brit. Med. Journal*, 7 juillet 1923.
- Duryea, C. F.**—A conservative Estimate of Radium in Gynecology. *Practice in Radium* compiled by American Institute of Medicine, 1922, p. 43

- Dustin, A. P.**—Contribution à l'étude radiologique des épithéliomas du col utérin traités par la télécuriethérapie. Contribution à l'Académie royale de Médecine, Bruxelles, 1927.
- Eisen, P.**—Clinical Features as the Determining Factors in the Application of Radium and Roentgen Rays in Malignancy. In International Medical and Surgical Survey, Sec. 10, 77-78, vol 11, 1921.
- Ewing, J.**—Analysis of radiation therapy in cancer: In Radium Report of the Memorial Hospital, New York, Hocker, 1924.
- Ewing, J.**—Tissue reactions to radiation. The American Journal of Roentgenology and Radium therapy, Feb. 1926, 93-115.
- Ferroux, R., Monod, O., Regaud, C.** (Paris).—Traitements des cancers du col de l'utérus par des foyers extérieurs de radium à distance. Jour. de Radiol. et d'Elect., 1925, vol. X, fac. 1, 1925.
- Furst** (Zurich).—Die Vorbestrahlung bei Kollumkarzinom des Uterus und ihr Einfluss auf die postoperative Infektion aus endogenen Ursachen. Zentralf. Gyn. 1925 N. 5 iss Wetterer Internationale Radiotherapie 1926.
- Giraud, M., Giraud, G., et Pares, L.**—Recherches expérimentales sur la genèse de la crise homoclasique des irradiations intensives. Presse Médicale, Paris, 1922, XXX, 885-887.
- Gosset, A., et Monod, O.**—Paris Méd., 16 février 1924.
- Healy, W. P.**—Evaluation of treatment of Carcinoma of the cervix with Radium. The American Journal of Roentgenology, Dec. 1925.
- Heymann, H. V.** (Stockholm).—Technik und Ergebnisse bei der Behandlung des Cervixkarzinoms mit "Radiumhemmet", Stockholm Strahlent., 1925, Bd. XX, S. 35. in Wetterer Internat Radioth. 1925-26.
- Huard, S.**—Cancer de l'utérus — p. 570-571. Paris Médical, 18 juin 1927.
- Hartmann, H.**—Sur la curiethérapie du cancer utérin. Rapport Masson, Paris, 1921.
- Kaplan, I. I.**—Radiation treatment of Malignancy of the cervix. Radiology, October 1927.
- Klemperer.**—Histopathologic changes in uterine carcinoma treated with radium. Am. Journal of Obst. and Gy., May 1925.
- Kok et Vorlaender** (Fribourg Bressgau).—Recherches biologiques sur l'action de l'irradiation sur le carcinome. Strahlentherapie Bd. XV, H. 5, 1923.
- Laborde et Wickham.**—Bulletin de l'association française pour l'étude du cancer. T. XV, No 7.
- Laborde, S.**—La curiethérapie des Cancers. Paris, Masson, 1925.
- Laborde, S.**—Journal de Radiol. et d'Elect. Paris, août 1922.
- Lacassagne.**—Microbes et phagocytes dans le champ du rayonnement. C. R. de la Soc. de Biologie, Paris, 14 mai 1921.
- Lachapelle, A.**—Contributions à l'étude des radionécroses tardives. Thèse Paris, L. Maloine.
- Laborde et Wickham** (Paris).—Radiumthérapie du cancer du col de l'utérus. 49e congrès de l'A. F. A. S., Grenoble, 1925.
- Lahn, W.** (Dresden).—Die Strahlenbehandlung des Kollumkarzinoms. 1925, pp. 567-571, in Wetterer Internat. Radiol. 1926.

- Lefulle.**—Action du radium sur l'utérus cancéreux. Presse Médicale, Paris, 11 fév. 1922.
- Ledoux, Lehard et Jean Gagey** (Paris).—Des rayons X et le Radium en gynécologie. Jour. de méd. et de chirurgie pratiques. Juillet 1923, pp. 480-496.
- Loeb, L.**—The effects of Roentgen Rays and radioactive substances on living cells and tissues. Jour. Cancer Research, 1922, VII, 229-282.
- Madr, Joseph.**—Radiotherapy of Cancer of the uterine cervix. Radiology October 1925.
- Mutermilch, S., et Lavedan, J.**—Traitement des infections secondaires des cancers, et, principalement des cancers du col utérin, par les auto-vaccins locaux. Soc. Biologie Paris, 30 juin 1923.
- Millet and Mueller.**—Some Phases of Radium Action with Special Reference to the Hematopoietic System. Jour. Cancer Research, 3, 127, 1928.
- Newcomet, W.**—Radium and the Roentgen Rays in Radiotherapy; Their uses and limitations. J. A. M. A. 63: 743-47. Aug. 29, 1914.
- Nogier.**—Le traitement des néoplasmes par aspiration osmotique. Avenir Médical, juillet et août 1923.
- Nogier.**—Considérations sur le traitement par le radium et la technique d'application dans les néoplasmes du col et du corps utérin. Paris Médical, 7 fév. 1920.
- Pochin, R.**—Désinfection des cancers ulcérés du col utérin par l'auto-vaccinothérapie locale. Paris, 1925.
- Pratt et Sokoloff, B.**—Contribution à l'étude de l'action des Rayons X sur les tumeurs malignes. C. R. Soc. Biologie, 13 octobre 1923, p. 735.
- Philip, E., und Gorwick, P.**—Die Behandlung des Gebärmutter und Scheidenkrebses an der Universitäts Frauenklinik Berlin. Munch. med. Wochenschr 1926. H. 7 in Wetterer Inter. Radioth. 1926.
- Perthes, J.** (Tulange).—La biologie et la clinique dans la Roentgen-thérapie des cancers chirurgicaux. Strahlentherapie, Bd. XV, H. 6, 1923.
- Proust et Mallet.**—Des indications respectives de l'hystérectomie, de la curiethérapie et de la radiothérapie pénétrante dans les cancers du col de l'utérus. Presse Médicale, Paris, 1er fév. 1922.
- Proust, R.**—Curiethérapie et Radiothérapie chirurgicale. 1924, Chanine, Paris.
- Quigley, Q. E.**—Irradiation in cancer of the cervix. Radiology, July 1925.
- Ransokoff, J. L.** (Cincinnati).—Radium in the treatment of cancer of the uterus. In "Radium", compiled by American Inst. of Medicine, 1922, p. 50.
- Recassens.**—Etat actuel de la radiumthérapie et de la radiothérapie dans le cancer de l'utérus. Presse Médicale, Paris, 1er fév. 1922.
- Regaud, C.**—Traitement des cancers du col de l'utérus par les radiations. Bruxelles, Imprimerie médicale, 1926.
- Regaud, Lacassagne, Roux-Berger, Coutard, Monod, Pierquin, Richard.**—Traitement des cancers du col de l'utérus par les radiations. Paris Gynéc. Obstétrique, 1925, vol. XII, No 4.

- Regaud et Coutard.**—Résultats et technique de la Roentgenthérapie dans les cancers du col de l'utérus. Gynéc. et Obst., Vol. XII, No 4, 1925, Paris.
- Regaud, C.**—Fondements physiologiques et techniques de la radiothérapie des cancers. Rueil Chantine 1921.
- Richard.**—Traitement du cancer du col utérin par le Radium. Paris Médical, 17 janvier 1922.
- Roussy, G., Laborde, S., Leroux, E., et Peyre, E.**—Bull. Ass. Francé Cancer XV, No 7, p. 431, et XII, p. 178.
- Roussy, G.**—L'état actuel du problème du Cancer. Paris, Gauthier Villars, 1924.
- Rubens Duval, H.**—La Curiothérapie est-elle une méthode dangereuse ? In Radium Report of the Memorial Hospital, New York, Hoeber 1924. Paris Chir., 13, 180, avril-mai 1921.
- Salomon, I.**—Radiothérapie profonde. Masson, Paris, 1926.
- Schneider, C. H.**—L'hyperthermie après le traitement par le Radium et les Rayons Roentgen. Strahlentherapie Bd. XV. H. 4. 1923, p. 550.
- Schmitz, H.**—Observations on the technique and Indications of Radium Therapy in Uterine Carcinoma. Surg. Gynec. Obst., 177, 1920.
- Schmitz, H.**—Contribution complémentaires à la valeur thérapeutique du Radium dans les cancers pelviens. Radium, vol. 2, octobre 1926.
- Schmitz, H.**—The relation of the degree of the histological malignancy to the prognoses and treatment of carcinoma of the uterine cervix. Radiology, Oct. 1927.
- Sherwood, Moore (St. Louis).**—Radiothérapie pénétrante. J. A. M. A. No 4, 28 juillet 1923.
- Sirédey et Gagey.**—Le Radium en gynécologie. Expansions Scientifiques, Paris, 1922.
- Schmitz, H.**—The treatment of Cancer of the uterus. J. A. M. A., 77, Oct. 8, Aug. 20, 1921.
- Skinner, E. H.**—Collateral Treatment of Malignant Patient Undergoing Radiotherapy. Am. Soc. Roentgenal 8, 138, mars 1921.
- Stacy, L. J.**—Complications qui suivent l'emploi du Radium en Gynécologie et discussions par H. Norsworthy, Chicago, C. F. Burnan, Baltimore, W. P. Healy, New-York, H. Schmitz, Chicago. Le rapport du congrès de l'Am. Radium Soc. à Washington, mai 1927.
- Stone, W. S.**—X Rays and Radium in treatment of malignant neoplasma.
- Taussig, F. J.**—Irradiation in cancer of the cervix. Radiology, July 1925.
- Villard et Michon (Lyon).**—Comment doit-on concevoir actuellement le traitement du cancer du col de l'utérus. Lyon Méd., 15 fév. 1925.
- Weil, René (Paris).**—Les accidents dus au radium dans le traitement du cancer du col utérin par la voie vaginale. Jour. Méd. Paris, 31 janvier 1925.
- Wintz, H. (Erlangen).**—Discussion on carcinoma of uterine cervix. Radiology, Oct. 1927, p. 329-30.
- Zweifel, E.**—The result of Radiations in case of uterine carcinoma. The Brit. Jour. of Radiology, Sept. 1927.



**Presentation of a Case of Prickle-
Cell Carcinoma of the Penis
Treated by Diathermy
and Radium.**

By B. C. CORBUS, M. D., F. A. C. S.

Chicago, Illinois

Chief of Staff, Illinois Social Hygiene Dispensary



Reprinted from the April, 1921 issue of The
American Journal of Clinical Medicine.

Presentation of a Case of Prickle-Cell Carcinoma of the Penis Treated by Diathermy and Radium

By B. C. CORBUS, M. D., F. A. C. S., Chicago, Illinois
Chief of Staff, Illinois Social Hygiene Dispensary

ACCORDING to Hazen, the researches of Krompecher and Bloodgood have definitely established the fact, both chemically and pathologically, that tumors arising from the superficial epithelium are of two varieties, prickle-cell and basal-cell.

The prickle-cell carcinomas are most common on the mucous membranes, especially of the lip. They form the vast majority of all cancers of the extremities and may occur anywhere on the cutaneous surface.

The relative frequency of carcinoma of the penis, compared with its appearance on other parts of the body, has been estimated as being from 2 to 3 percent.

Location

Prickle-cell cancers arise most frequently from either arsenical or Roentgen-ray keratoses and, according to Hazen, less frequently from scars due to burns or wounds that have healed by granulation, from leg ulcers, from wens and from various chronic dermatoses. This is especially true in cancer of the penis, where the tumor begins on the glans or inner leaf of the foreskin as a result of a chronic balanoposthitis with resulting retained smegma and decomposing urine.

Appearance

Nothing can be added to the description of these tumors, as they have been well described and studied by numerous observers, prominent amongst whom are Barney and Cunningham.

Metastasis and Pathology

Prickle-cell carcinomas, as a rule, metastasize to the regional lymphatics, although this may not take place for years; from here, metastases occurs to the lumbar glands along the vertebræ and here the condition may be dormant for a long time, later springing into activity.

Gross Pathology.—When a prickle-cell cancer is excised and cut through, three things are to be noticed: first, that the

surface is rough; second, that the infiltration is deep; third, that the cancerous alveoli radiate downward in the form of white lines, about the size of a very fine thread.

Microscopic Pathology.—When a section from a prickle-cell carcinoma is stained with hematoxylin and eosin or with a similar combination of acid and basic dyes, it is noted that the cancerous alveoli are large, and that there is a great tendency for whorl formation to occur. These whorls are very apt to result in epithelial pearls. In addition, the individual cells are large and stain intensely with the acid dyes.

Diagnosis

The solution of the cancer problem lies in the early recognition of the disease and its adequate treatment. This can be best accomplished by educating the medical profession to recognize it in the early stage, and the laity, to seek early advice.

With an early diagnosis and with immediate and proper treatment, the prognosis is excellent. In late diagnosis, even with skillful treatment, the prognosis is fatal. If hematuria had the same effect on the physician and layman as hemoptysis has, few tumors of the urinary tract would go undiagnosed.

According to the best authorities, under no circumstances should a section of a growth be removed for diagnosis by simple excision; for, such a procedure leaves the blood vessels and lymphatics gaping and favors the dissemination of the cancerous process, in as much as malignant cells can readily enter the circulation.

Of late years, the procedure of diagnosing genital ulcers has been so well established, by the process of elimination, that it should not be difficult to recognize a cancerous condition without excising a piece of tissue for diagnosis.

Treatment

The treatment of cancer depends upon

the diagnosis. The earlier a diagnosis is made, and treatment instituted, just so much more promising is the prognosis.

So discouraging has been the treatment of cancer by the knife, that the growing tendency, especially in bladder tumors, is to avoid any procedure that might produce metastases.

Beer, in his recent contribution to the operative treatment of neoplasms of the urinary bladder, says that it is necessary, in working out a technic, to keep constantly in mind that every step of the operation must be worked out so as to avoid implanting tumor cells on raw or cut surfaces. The same holds true in cancer of the penis.

In order to avoid any cutting procedure, many methods have been advocated, chief of which are, cauterization by the hot iron; still later, electrical desiccation or coagulation, together with ferments or enzymes.

What promises to be the most successful method of treatment is massive electrical coagulation by means of diathermy.

For the benefit of those who do not understand what diathermy is, the following passage, quoted from Claude Saberton on "Diathermy in Medical and Surgical Practice," just issued, may be of interest.

"Professor Zimmern, of Paris, has defined diathermy as 'a form of thermotherapy which utilizes electrical energy for the production of thermal effects in the depths of the tissues.'"

In order to raise the internal temperature of the body, we must employ currents which reverse their direction many thousands of times per second, i. e. high-frequency currents.

Franz Nagelschmidt, of Berlin, modified and developed the high-frequency machine in order to obtain marked thermal effects, and called the treatment "diathermy."

He demonstrated a diathermy apparatus designed by himself and, in 1907, at Dresden, he demonstrated the "heating-through" of tissues by high-frequency currents, suggesting their use in the treatment of diseases of the circulation and the joints. In 1908, a joint paper, written by von Berndt, von Preiss and von Zeynech, laid stress on the diathermic effect of high-frequency currents and advocated their use in the treatment of joint diseases. In 1910, Eugene Doyen communicated to the International Congress of Physiotherapy an account of the treatment of cancer by means of electrically-produced heat."

While diathermy has been used on the Continent and in England for some time, the American surgeons seem to be far be-

hind. However, to Dr. Gustave Kolischer belongs the credit for first using and demonstrating its wonderful effect in destroying cancer tissue, in this country.

Norman Patterson, writing in the *Lancet* (London), December 6, 1919, says "No excision of a carcinomatous growth in the tongue, mouth or pharynx, however small that growth may be, should be carried out with the knife if diathermy is available."

The Case History

The case which I present has the following history:

M. T., 40 years old, Chicago.

Family History.—Father died at 70 of unknown cause. Mother died at 69 of unknown cause. One sister died at 56 of alcoholism. Two sisters living and well. One brother living and well. No carcinoma, tuberculosis or insanity in the family.

Marital.—Married 15 years. Wife always well. Two children living and well. Two children died in infancy of contagious diseases. Wife had no miscarriages or stillbirths.

Habits.—Eats—well; sleeps—well; alcohol—none; tobacco—moderately; drugs—none.

Past History.—Always well until present illness. No diseases of infancy. Accidents—none. Operations—none. No other generalized symptoms. No headaches, edema, cardiorespiratory, gastrointestinal or neuromuscular complaints.

Genitourinary.—No gonorrhea or syphilis. No frequency or dysuria.

Present Illness.—Onset.—Five years ago, a small wart-like growth appeared just beneath the foreskin in the sulcus coronarius, on the ventral surface. Patient had a persistent phimosis for years before this. He consulted Dr. X. Y. Z., who circumcised him, at the same time removing the growth.

Course.—Following circumcision, which was done on March, 1916, the skin all around the penis failed to heal and became infected, followed by a profuse yellowish discharge. This continued for 3 years. No treatment other than boric acid applications was ever given. After two years, the granulation tissue about the old incision began to become hard and nodular and to heap up. This gradually continued until the growth became as big as a small orange. The patient worked up to August 1920, when he had to give up going about because the odor from the lesion became so disagreeable. During all this time, his general health was excellent and he had no urinary or rectal symptoms at any time.

Glands.—Never swelled up or became tender until June, 1920. At this time, the growth was very necrotic and sloughing. The glands enlarged very gradually until they were the size of a large pigeon's egg.

Destruction of Tumor by Diathermy.—This was done by myself at the Evanston hospital on October 7, 1920. Dressings of

vaseline continued. Slough separated completely on the tenth day leaving a clean granulating surface.

X-Ray.—Two x-ray treatments were given over the groins during the last days of October.

Radium.—November 1, radium treatments (four in number) were given by Doctor Hanford. Severe reaction in inguinal glands and about penis, followed by marked cleansing of granulation tissue and increased vascularity to areas about edges.

Radium needles were inserted into either groin for 8 hours at C. C. H. by Doctor Hanford, with marked reaction about granular enlargement.

Examination, March 15, 1921. Improvement is so marked and tissues are so free

from noticeable cancer-tissue, that a skin-grafting operation is performed.

Conclusion

While nothing spectacular is expected in a case that has gone for four years without a diagnosis, it was interesting to see how easily this enormous fungating mass could be removed with diathermy and replaced by healthy granulation tissue.

By the diligent application of radium, what remained of the cancer tissue and the inguinal metastases, has greatly improved; but, unfortunately the deep common iliac vessels are already involved.

TECHNIQUE OF RADIUM TREATMENT FOR LUPUS ERYTHEMATOSUS

H. W. P.

BY

GEORGE D. CULVER, M. D.,
SAN FRANCISCO, CAL.

Reprinted from "*Radium*," Vol. 3, New Series, No. 1

April, 1924.

TECHNIQUE OF RADIUM TREATMENT FOR LUPUS ERYTHEMATOSUS

BY GEORGE D. CULVER, M.D., San Francisco, Cal.

Dermatologists regard failure to cure lupus erythematosus as in the natural course of events, and among them it gives rise to no unfavorable criticism. With the general profession, however, it is different, for the disease is regarded as a superficial affair and failure in treatment is looked upon as an indication of the weakness of dermatology as a specialty. As for the laity, an unfavorable issue is particularly unfortunate, as the lesions are almost always on the face, more frequently in women, and they constitute a continual reminder of our deficiencies.

The reputation of radium in the management of lupus erythematosus was one of the factors that stimulated our investment, and before long the purchase for this use was regarded as of doubtful value. This doubt was really due to faulty technique. A later method proved much more satisfactory.

Half or full strength plaques of radium have proven best, screened with sufficient metal and additional distance screening, as with rubber or paper, to eliminate all the alpha particles and many of the less swift beta ones. To illustrate: A plaque two centimeters square, containing ten milligrams of radium element, is screened with 0.2 to 0.4 millimeters of lead and eight to twelve layers of writing paper, or 1 to 2 millimeters of rubber. The plaque is left in place for from two to two and a half hours, covering a little beyond the edge of the lesion. This exposure is followed by some redness and often by superficial necrosis, which, however, is late in appearing—about eight or ten days after the exposure. The superficial necrosis heals quickly.

The prolonged irradiation probably acts on the deeper blood vessel walls, and on the endothelial cells.

There is still another effect produced. As is well known, radium, if unscreened or only lightly screened, gives rise to permanent capillary dilatation. Employed in the above way, however, it not only has not caused this disfiguring capillary dilatation, but many of the capillaries resulting from the disease and from previous, more lightly screened irradiations have disappeared.

It was not until the latter part of the year 1920, after having used radium for nearly five years, that I began to employ the heavier screening mentioned above, and the longer exposures; and not until the earlier part of 1922 that I was completely convinced of the marked superiority of this method. The results are far beyond anything attained by any other local means within my experience.

Of course, the use of radium does not preclude measures looking to the general health of the patient and the employment of other remedies locally, such as pure alcohol vigorously rubbed in, or an alcoholic lotion consisting of:

Salicylic acid	1.00	Essence of Lavender	10.00
Acid boric	10.00	Spts. vini rect. (95%) ad	240.00

which Dr. Corlett once kindly suggested for use in acne, and which is excellent. Hutchinson's lotion in different strengths of dilution also acts well. Frequently the hyperkeratoses clear up after the use of

trichloroacetic acid. As is well known, salves do not act well in this disease.

The main local treatment, however, is now with radium. It almost never fails to accomplish some good with each application, and where possible to repeat the irradiations at intervals of from six weeks to two months it is the exceptional instance that will resist its effect and fail to disappear.

Local treatment in the past was by no means an entire failure. However, the disease was far from being a joy to treat. It was not a simple matter to judge therapeutic results, as lesions would disappear without treatment or in spite of it. Only by grouping stubborn cases has it been possible to reach a satisfactory conclusion as to what to expect from irradiations with radium.

In a group of ninety-eight cases of lupus erythematosus, dating back seventeen years, just half that number have been treated with radium irradiations, and of the forty-nine, thirty-eight have come under supervision at some time since the first of 1920, that is, during the last four years, and since using radium more heavily screened. Twenty-six of the thirty-eight show excellent effects from the radium irradiations as described above, and sixteen of this number show quite satisfactory end results. Of the remaining portion of the thirty-eight cases some are those recently acquired who are under treatment and others have continued their nomadic tendencies.

One finds gratification in having a method of procedure that is so effective as to hold as nomadic a group of patients as those afflicted with lupus erythematosus. It is also a satisfaction not to dread their visits.

Citation of individual cases would be a time consumer without sufficient recompense. One instructive instance may be mentioned, that of a woman forty-one years old, who in 1912 had had lupus erythematosus three years. I first saw her in September of 1912, and from time to time until February of 1916, when she quite justifiably sought help elsewhere. June 5, 1922, more than six years later, she maneuvered through another member of her family to get me to call at her home, because her face was so extensively covered with active lupus erythematosus patches she dreaded appearing in the office. She would appear on the street only when so heavily veiled her face could not be seen. Irradiations were immediately begun. Four plaques of radium (one 2x2 centimeters square plaque containing 10.86 milligrams of radium, another of similar strength somewhat larger, and two 25 milligram plaques of the size of a ten cent piece, the weaker plaques being screened with 0.2 lead and twelve layers of paper, the two stronger plaques with 0.4 lead and sixteen layers of paper), were applied for two hours. Fourteen sittings with not more than four applications in any one place, have so nearly freed her from eruption that only indefinite areas indicate further treatment.

Her lupus erythematosus was of the type that left scarring in all situations, and on the scalp denuded the patches of hair. It affected the eyelids, extending on to the edges, the lips extending on to the mucous membranes, with other patches running into the nostrils and also affected the meati of the ears.

Most of the dilated capillaries that were present have disappeared.

This case was the type that in the past I should have desired someone else to have the responsibility of treating. That, however, is not now the attitude of mind I feel in reference to even the most discouraging picture.

RADIUM IN THE TREATMENT
OF UTERINE HEMORRHAGE OF
NONMALIGNANT TYPE

By

EDWARD A. WEISS, M.D., F.A.C.S.,
Pittsburgh, Pa.

From the Gynecological Department, Mercy
Hospital

Reprinted from

THE AMERICAN JOURNAL OF
OBSTETRICS AND GYNECOLOGY
St. Louis

Vol. V, No. 2, February, 1923

RADIUM IN THE TREATMENT OF UTERINE HEMORRHAGE OF NONMALIGNANT TYPE*

BY EDWARD A. WEISS, M.D., F.A.C.S., PITTSBURGH, PA.

(From the Gynecological Department, Mercy Hospital)

FOR several years there existed considerable skepticism in the minds of many as to the permanent value of radium in the treatment of uterine bleeding. The careful studies of John G. Clark, Bailey, Stacy and others have established beyond any reasonable doubt the efficacy of radium in the treatment of certain types of profuse bleeding of nonmalignant origin. The brilliant results obtained in some cases having been so pronounced, it is not surprising that the procedure would be abused by inexperienced persons using radium when not indicated, with the result that unfavorable reports have frequently been published.

With the broad experience of physicians and gynecologists of note to guide us, there should be no question as to the real merit of radium, and failure to appreciate it as a valuable therapeutic agent can be attributed to either prejudice or lack of experience. It is a fair assertion to make that no gynecologist is justified in withholding his willingness to consider the employment of radium in the treatment of selected cases of uterine bleeding. At the same time we do not subscribe to the statement that radium has supplanted surgery in the treatment of fibroids as in all probability there will still remain a large percentage of tumors requiring operation.

So convincing and complete are the reports of Clark and Norris in a recent analysis of their radium work that further comments would seem unnecessary, and while very little can be added to their conclusions, the reports from other clinics should be added to our gynecologic literature. A most careful and honest follow-up of the work from various gynecologic clinics should be tabulated for a long period of time in order to establish the status of radium and in a measure standardize the treatment. Our series of cases analyzed in this paper bear out to a large extent the observations of others. The results obtained were sometimes surprising and accomplished with wonderful ease as compared with operation, yet a critical attitude should be maintained and enthusiasm and optimism should not wean us from the well established operative treatment so successfully practiced for many years.

A series of one hundred cases in which bleeding was the only or

*Read at the Thirty-fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Albany, N. Y., September 19-21, 1922.

chief symptom, were selected for this study. It does not include our early cases when the technic was not definitely established and when mistakes in the selection of cases occurred, nor does it include cases treated during the past six months as not sufficient time has elapsed to tabulate these end results. In this group were eighty-three cases of submucous or interstitial myoma, four of adolescent bleeding with no pathologic findings and thirteen of functional menorrhagia or myopathic bleeding. Curettement as a diagnostic measure to exclude malignancy was performed and a careful selection of cases for radium treatment was made in every instance. When any doubt existed, operation was resorted to rather than radiation. With the exclusion of such doubtful cases, it follows that very few untoward or unsuccessful results were obtained. A rigid standard of indications and contraindications must be adhered to in order to obtain uniform results. The technic in every case was practically the same. The patient entered the hospital twenty-four hours before treatment, during which time the same careful physical examination was made and all routine urine, blood and Wassermann tests were completed, and the usual preoperative preparations likewise followed out. As the cervix is usually soft and patulous in these patients, due to the existing or previous bleeding, it is easily dilated, in which case an anesthetic is generally not necessary. In very nervous individuals the administration of morphia one-half hour before treatment was often sufficient, but in the presence of a rigid hymen or firm cervix, gas-oxygen was given. The depth of the uterine cavity, the size, mobility and consistency of the fundus was noted, a careful palpation of the adnexa made, a formal curettement was done and the curettings preserved for microscopical study. Radium needles of appropriate dosage, usually fifty mg., are screened in 2 mm. brass capsule and rubber tubing. Firm gauze vaginal packing to maintain the screened radium in the uterus is essential. In the average case the patient was kept in bed two or three days, but those more debilitated by long continued bleeding remained in the hospital longer in order to build up the general condition.

Eighty-three cases of the study were bleeding myoma. In selecting myoma cases for treatment, only those that were not larger than a three months' gestation were included. Intraligamentary or degenerating tumors were not considered suitable for radium. In spite of some favorable reports from other clinics, pedunculated tumors were also excluded in this series, likewise those suggesting degenerative changes were reserved for operation. Any evidence of inflammatory changes in the adnexa, either acute or chronic, contraindicated radiation. It has been repeatedly pointed out that chronic or latent adnexal inflammations are frequently excited to fresh reaction following

radium treatment. In our earlier series, two such instances were encountered with the result that a protracted convalescence ensued, after which radical operation was necessary. Six instances of rather large submucous tumors in uteri containing interstitial nodules were encountered. These projecting tumors were removed either by torsion or removed through a split cervix. In these cases the bleeding would in all probability have been arrested by operation alone, but radium was used not only to reduce the large, flabby uterus but to have an inhibiting effect on the remaining nodules. Curettings from one case showed an unrecognized carcinoma of the fundus. Radium had been introduced at the same time as polypoid endometritis had been diagnosed from the gross appearance. As we believe that fundal carcinoma is best treated by hysterectomy, radical operation was advised but this was refused by the patient. Repeated examinations have shown no recurrence of the bleeding after two and one-half years and it is fair to assume that the disease was arrested.

The most spectacular results were obtained in eight cases in which the blood picture was that of a severe secondary anemia due to bleeding myomata. Three of these cases presented a hemoglobin below thirty-five with accompanying low general physical picture contra-indicating operation. Before the advent of radium in our therapy, such cases would of necessity require blood transfusion and much preoperative attention. With radium, the arrest of the bleeding was prompt with a rapid improvement of the patients' general condition. Two cases of this group of eight had a return of the bleeding within a year. The tumor had not decreased greatly in size but the condition of the patient was so good that hysterectomy was easily and safely performed.

In addition to the two cases mentioned, one other required operation, not on account of recurrent bleeding but for relief of persistent and aggravated pelvic pain, associated with occasional temperature. Operation disclosed an unrecognized secondary pyometrium due to unusual contraction and stenosis of the cervix following the radium. This is the only instance of its kind encountered. Some authorities believe that radium exerts its influence largely on the endometrium as well as on the ovaries. The mucous membrane of the uterus is destroyed by the direct effect of the secondary beta rays and while microscopical examinations of the endometrium in uteri removed after radium application have shown no definite necrotic changes, yet it is reasonable that such should occur. In discussing the action of radium on the uterus, Schmitz states that part of the endometrium receives an erythema or a first degree burn, another part a second degree burn and the portion in the immediate surroundings of the radium a third degree burn. Imperfect drainage through the cervical canal would

favor retention of the debris, and so favor the formation of pyometra. Since the occurrence of this complication in our series, it is the rule to explore the cervical canal to test its size and pathological state in all cases developing symptoms such as temperature or softening of the fundus after radiation.

Great care was exercised in using radium in women under thirty-five and whenever it was used, only minimum dosage was given. It is generally admitted that in women in the child-bearing age, myomectomy is the better method of treatment as it is not infrequent that even a moderate dose of radium produces menopause. In treating women who can and should have children, the child-bearing function of the uterus should be preserved. In this connection we venture to condemn in unmeasured terms, the unscrupulous and unprofessional employment of radium as a direct means to prevent conception by producing a premature menopause especially when no pathology is present.

The unexplained uterine bleeding in adolescence and young women has often taxed the skill of gynecologists, and its unsuccessful treatment has resulted in many deaths. Numerous explanations have been offered for this peculiar type of bleeding and while hyperfunction of the ovary has been generally accepted as a causative factor, yet the various remedies as glandular extracts, serums, styptic and curettements fail to arrest the bleeding. In the past, hysterectomy has often been resorted to in order to save the young woman's life, but the unfortunate sexless life of the individual resulting, is sometimes worse than death. With the advent of radium, an almost specific has been obtained, and while radium is more applicable in women at or near the menopause on account of the large dosage employed, yet with care and judgment, the excessive bleeding of the pubescent girl can be reduced and regulated. In our series four instances of profuse and almost uncontrollable bleeding were encountered. In one case the patient, a fourteen year old schoolgirl, with excellent physique and negative history, had three normal menstrual periods after which the flow became excessive and prolonged. Rest in bed, forced feeding, animal serum, various medications and uterine packing had little or no effect. The blood picture became so alarming that even hysterectomy could not be attempted. The insertion of 25 mg. radium screened in the uterus for eight hours arrested the bleeding and produced an amenorrhea for six months, after which the last two periods have been somewhat more profuse but the general condition and blood picture are practically normal.

A young woman of twenty-eight (a case of hemophilia) who bled excessively had been previously transfused. With a return of the uterine bleeding, radium was proposed and as she refused to submit

to the production of menopause, a minimum dose of 150 mg. hours was given. Great improvement was noted for six months with practically normal menstruation. After two rather free bleedings a second dose of 150 mg. hours resulted in a return to normal. A third case less severe in type required three doses of 25 mg. each for six hours before the menses became normal. It seems more conservative to resort to repeated small doses in young women rather than employ a single large dose. In other words a dosage of 1200 mg. hours can safely be used once in a woman after forty with pronounced result, yet in a young woman, 200 mg. hours used once or even three times if necessary would be efficient, and yet not necessarily rob her of the possibility of motherhood. Pregnancy has not occurred in any of the cases treated, yet with normal menstrual function, such possibilities are very favorable. Clark, Stacey and others have reported several instances of pregnancy following radium in minimum dosage, so that it is most important to keep such possibilities in mind when treating women in the child-bearing age.

The action of radium in controlling bleeding in myoma and myopathic conditions is an interesting study. Several explanations have been offered. Bailey believes it exerts its influence in three ways: (1) by action on the ovaries causing a destruction of the primary follicles. This would lead to a failure of ovulation and a consequent cessation of menstruation and would possibly lead to a retrogression of the growth similar to that which often follows the menopause. (2) By the destruction of the mucous membrane of the uterus through the direct effect of the primary and secondary beta rays. (3) By the effect of the gamma rays on the blood vessels leading to an occlusion or partial occlusion of their lumen.

Bleeding at the menopause in the absence of carcinoma, fibroid or other pathologic condition not infrequently gives rise to much concern both to the patient and physician and while this idiopathic bleeding rarely assumes serious proportions, yet the fear of possible malignancy is such that prompt relief is frequently demanded by the patient. In four of this series, the menorrhagia and metrorrhagia were pronounced. Gross pelvic pathology as well as cardio-vascular disease were eliminated as causes. The ages of the patients were forty-six, forty-nine, fifty-two and fifty-three respectively. Fifty mg. radium for twenty-four hours produced a complete cessation in every case. Curettings showed no hyperplasia or malignant changes so that atheroma of the uterine vessels was doubtless the underlying cause of the bleeding. The results obtained in this type of menorrhagia frequently classified as hyperplasia, fibrosis, uterine insufficiency or chronic metritis are so satisfactory that no surgeon is justified in resorting to radical hysterectomy to obtain a cure. It is certainly

not acting for the patient's best interests if he does not employ radium if procurable.

Not included in this series were four cases of fibroid bleeding that had been treated in other clinics without relief. Analysis of the history showed that very severe localized peritonitis followed the radium introduction and it was quite evident that a pre-existing adnexal disease was renewed by the radium treatment. This experience demonstrated very forcibly that a careful diagnosis and study not only of the tumor but existing complications is most essential. It is true, therefore, that the gynecologist and not the internist or roentgenologist should employ radium in the treatment of pelvic conditions, as the success or failure of its application depends primarily upon a correct and complete diagnosis.

In all cases receiving full dosage in this series, forty were relieved at once without return of the bleeding. Thirty-five menstruated once, fifteen menstruated three to five times, ten received two treatments. The irregular bleeding for the first ten days after treatment is not to be attributed to the radium but rather to the effect of the curettement, if not due to the disturbance of the ovarian hormone. It has been noted that a larger percentage had leucorrhea in varying amounts for the first two to five months. Frequently it has been very annoying and irritating, but generally is best relieved by douches of bicarbonate of soda. Probably the most annoying sequelae in our series has been nausea and vomiting while the radium is *in situ*. In many instances, it was attributed to the preliminary doses of morphia in those patients who were not anesthetized. However, the nausea was present in eighteen cases who received neither morphia nor gas, so that we have designated it "radium sickness" for want of a more definite explanation.

The decrease in the size of the uterus was generally not manifest before the tenth week after which the shrinkage became more pronounced. As a general thing, the menopause symptoms were more acute following radium than occurs normally but in most instances the administration of ovarian residue or corpus luteum helped to reduce the severity of the symptoms. The possibility of producing the menopause even with minimum dosage should be explained to the patient, especially younger women. In one instance the use of fifty mg. for six hours in a patient thirty-two years old produced a permanent amenorrhea with unusually severe menopause disturbance. The mental depression and disappointment was so acute that a serious nervous collapse followed, from which she is very slowly reacting but the sexual function is completely inhibited. The splendid results following radiation of fibroid tumors has unfortunately resulted in such a degree of optimism in some quarters that it is used in almost

every type of uterine tumor. This is most unfortunate as its indiscriminate use will often result in failure or aggravation of existing pathology. Only in exceptional circumstances as in the presence of serious heart or kidney lesion or grave constitutional disturbance when an operation would be extremely dangerous, is a deviation from the well established indications justifiable. The employment of radium to reduce a tumor larger than a three months' gestation is fraught with a certain degree of danger, neither should it be used in a tumor causing pressure and whose structure is purely fibroid or a dense hyaline or calcareous structure. It is granted that shrinkage of such tumors sometimes occurs, but with our present knowledge of distinct indication and contraindications the careless use of radium is not justified. Neither do we countenance its indiscriminate use to control uterine bleeding that is secondary to pyosalpinx or other adnexal disease. To clearly define our position therefore it may be stated that in our work the most satisfactory results were obtained in the treatment of one symptom only, namely hemorrhage, and we feel positive that radium used with care and clear discrimination has undoubted merit, acting almost as a specific and possessing the additional advantage of having almost negligible objections.

CONCLUSIONS

In the treatment of benign hemorrhage from the uterus the following observations are to be considered:

1. Radium should be used only in selected cases such as (a) myopathic bleeding of adolescence that does not respond to usual medical and hygienic measures; (b) myomata with bleeding as a symptom that are of small or moderate size and uncomplicated by adnexal disease; (c) menorrhagia of menopause.
2. The dosage depends upon (a) the age of the patient; (b) upon whether the function of child bearing is to be preserved or sacrificed.
3. Myomectomy in young women, and hysterectomy when the tumor is large or complicated should be done rather than treatment with radium.
4. Complications and unfavorable results are to be avoided only by a careful discriminating differential diagnosis.
5. All cases treated by radium should be carefully followed up for several years.

714 JENKINS ARCADE BUILDING.

RADIUM CLINIC FOR TREATMENT
OF EYE, EAR, NOSE AND THROAT
CONDITIONS.
THE EFFECT OF RADIUM ON
GLAUCOMA.

BY

J. J. CORBETT, M. D.

Ophthalmic Surgeon, Boston City Hospital; Ophthalmic and Aural
Surgeon, Malden Hospital; Ophthalmic and Aural Surgeon,
Whidden Memorial Hospital, Everett.

RADIUM CLINIC FOR TREATMENT OF EYE, EAR, NOSE AND THROAT CONDITIONS.*

(From the Radium Clinic of the Eye, Ear, Nose and Throat Departments
of the Boston City Hospital)

At the Boston City Hospital, there was started in August, 1922, a clinic for radium treatment of some eye, ear, nose and throat conditions.

There is one outstanding and conspicuous feature about this clinic, namely, that easily 98% of the cases in which radium is used are non-malignant. This contrasts very markedly with the general use of radium to date, and with the accepted and prevalent idea carried in the lay or non-medical mind. The name of radium has been so intimately linked with that of cancer that it has almost become a synonym for malignancy; and yet, as radium becomes better understood and its uses more diversified, it will not be at all surprising if its application is not productive of more good in the non-malignant field. Its success will be measured not alone by what it accomplishes in a physical way, but in an economic way as well.

When the idea of such a clinic came to mind, it was accompanied by much doubt as to whether the project could be successfully carried out. Members of the executive and staff were approached and their co-operation enlisted. As a result of their enthusiastic efforts, there were provided cases upon which the work has been done to demonstrate the use of radium

Of course, the clinic is still in its infancy, and the work done to date is limited. In a short period of two and one-half months, several groups of cases were treated. These cases were shown at the Dry Clinics as part of the program arranged for the American College of Surgeons at the Boston City Hospital. As stated at the time, the cases were shown not with the idea of proving what radium would or would not do, but rather to call attention to the lines along which the work was being done.

To demonstrate the use of radium on tonsils, four cases of the hypertrophied variety were selected. The tonsils were of the large, spongy type that meet in the middle line. In each throat, one tonsil was treated, in order to show the difference between the treated and the untreated tonsil. The difference was very apparent. The treated tonsils were much shrunk and more firm, while the untreated tonsils showed only a slight change, undoubtedly due to stray gamma rays: Four 12.5 milligram needles were buried in the tonsil for fifteen minutes, once a week, for six consecutive weeks.

Reprinted by permission from the Boston Medical and Surgical Journal, etc., 1082-1084, June 19, 1924

Two of these cases were interesting, one from a systemic, the other from a local point of view. A man 38 years old, tailor, whose right tonsil was treated, offered the information that the pain in the right shoulder, from which he had suffered for several months, had entirely disappeared. He had received massage, electric treatments, and various internal remedies without relief. The interesting feature lies in the fact that the left shoulder which had been as painful as the right was not relieved by the treatment of the right tonsil, and showed signs of relief only after the left tonsil had been treated. The other case, a boy 14 years old, had difficulty in articulating, owing principally to the enormous size of his tonsils which met in the middle line. His speech was conspicuously muffled. After three applications of 50 milligrams of radium for fifteen minutes in each tonsil, there was a decided improvement in his speech, and now his articulation is quite normal.

Before beginning the treatment of tonsils by imbedding the needles into the substance of the tissue, other methods were tried. The needles were held against the oral side of the tonsil in some cases, and in others, applied externally, being screened in brass and hard rubber, and separated from the skin by 2 cm of gauze. Observation led to the conclusion that the quickest and most effective manner to use radium was in the form of needles plunged into the body of the tonsil and allowed to remain. Fifty milligrams of radium have been used for periods varying from fifteen minutes to one hour without any serious reaction, and repeated at weekly intervals.

It may not be amiss to state some of the impressions derived from the use of radium on tonsils. When anticipating the treatment of tonsils, radium should be given only secondary consideration. It is simply an instrument added to the armamentarium of the laryngologist, and should be used in selected cases. When the tonsils are diseased, or productive of systemic complications due to absorption from local infection, enucleation is the quickest and most effective method of treatment. If, however, operative treatment is contra-indicated, radium is the second choice, and may be resorted to with considerable confidence.

There are three classes of cases in which tonsillectomy is not desirable and in these radium may be used with success. These are (a) the physically unfit; (b) the mentally unfit; (c) the commercially unfit. Patients in class A will be met in the clinic and private practice. Patients in class B and C will be met practically at all times in private practice.

In class A will be found patients with organic changes which make them poor operative risks; patients whose histories point to haemophilia; suspicious cases of status lymphaticus in children; and adults of advanced years in whom all other possible foci of infection have been ruled out. Radium in these cases will give good results.

Class B includes the patient whose next door neighbor might have had a hemorrhage after tonsillectomy, or who has heard the gruesome story of someone who bled to death after a tonsil operation. Any complication whatever, whether a co-incidence, or a direct result of tonsillectomy, is apt to come to the mind of one who is anticipating such a step, and very often will result in a decision against the operation. The patient who dreads anesthesia more because of the loss of consciousness than of the anesthetic itself, or because he has heard of a death which occurred while tonsils were being removed, the patient never regaining consciousness, welcomes the suggestion of radium treatment.

Class C includes the busy man who cannot stop long enough for such a thing as an operation and convalescence from the same. He has been advised by his physician and his physician's consultants that his tonsils alone remain the only source of the infection which is causing his physical discomfort. He is physically fit, has all the courage in the world (and some to spare), he dreads or fears nothing. He would take ether with the same indifference as he would take a drink of water, but he simply cannot take a week or ten days away from his business for the sake of the operation. Such a man typifies class C, and he may look with confidence for relief from radium.

Enough work has been done with radium to warrant the recommendation of its use in such cases as are suggested in these three classes, and with the hope of getting good results locally and systemically. But if the condition of the patient warrants it, advise surgery first and hold radium as a second choice. Radium does not remove tonsils. It transforms them into small, firm fibrous lumps of tissue. In this shrinking process, the toxic material contained in the crypts must be squeezed out, and the tonsils rendered inert as sources of infection.

Aside from epitheliomata, the most interesting nose case which has come to the clinic was one of hemangioma of the septum. The patient came to the Nose and Throat Out-Patient Department, and pressure was applied to control the bleeding. There was temporary relief but the patient returned the next day and the nose was still bleeding. The patient was admitted to the House and suture applied. This gave temporary relief, but after two days, there was more bleeding. The patient was then referred for radium treatment. Examination showed a tumor starting from the muco-cutaneous margin of the septum and large enough to completely occlude the left nostril. There was a slight oozing of blood. Twenty-five milligrams of radium were applied for fifteen minutes. In two days, the same dose was repeated. One week later, the dose was given for a third time. At the end of three weeks, the tumor was shrunk to one-half the size of a buck-shot. There was no bleeding from the day of the first application of radium.

As the clinic has progressed, the number and variety of cases have markedly increased. The clinic has now been in operation about one year and a half. For the first few months, there was no restriction as to the type of case as long as it was of interest to the Eye, or the Ear, Nose and Throat Departments. Volume and variety were the two features developed, the idea in mind being to weed out the cases that would not respond to radium treatment. The volume increased so rapidly and the variety became so great, that during the past six months, it became necessary to restrict both volume and variety of cases.

Corneal scars and cataracts became the principal conditions upon which work was concentrated. At the April meeting of the New England Ophthalmological Society, held at the Massachusetts Charitable Eye and Ear Infirmary, seven cases were shown. Three of these were cataracts, one a congenital and the other two incipient senile cataracts. The vision of the eyes was taken with and without glasses, before and after the treatment with radium. Both cases showed an improvement of vision without glasses, and with glasses, could be brought to 20/20 normal. This had not been possible before the radium was applied.

The congenital cataract was in the right eye of a boy $3\frac{1}{2}$ years old. The cataract could be seen by the unaided eye. The pupil appeared gray

instead of black. There was no fundus reflex. Incidentally, there was a convergent squint in the same eye. After treatment, the pupil appeared black; there was a clear fundus reflex; the retinal vessels and optic disc could be seen with the Ophthalmoscope. The eye was refracted and a +1.00 Cyl. Axis 90 was prescribed. The convergance was overcome by the wearing of glasses. It is now eight months since the last treatment. The view of the fundus is still clear and the eye remains straight with the help of glasses.

In the four cases of corneal scars, there was a definite improvement in the vision after treatment with radium. Two of the very thinnest scars, (nebulæ of the cornea) entirely disappeared. The other two showed a very definite thinning out. There was a definite improvement in vision in each of the four cases shown.

Conclusions: That in certain selected cases of cataract, radium gives a definite help.

In cases of corneal scars which are not too dense, mostly nebulæ of the cornea, a clearing up of the scar, and an improvement in vision can be demonstrated.

That radium has a very definite action on tonsillar tissue which is far reaching in its systemic results.

That when tonsils cannot be removed by surgery, radium is the next choice.

THE EFFECT OF RADIUM ON GLAUCOMA*

To say the least, the use of radium is extremely fascinating. In most cases, the results come slowly, but occasionally the unexpected happens. Then one feels fully compensated for the effort and time put into the work.

The writer wishes to call attention to what he considers a spectacular result of radium treatment in one of the most serious of pathological eye conditions, namely, glaucoma. Three cases will be described.

1. Patient, A. C., male, 62 years old, consulted me on April 27, 1923. The patient stated that the vision had been failing in the right eye for over a year. He had been under treatment with other oculists and, on April 25th, the eye became suddenly blind. The eye felt sore but the pain was not severe.

Examination showed the right eye to be markedly injected, the cornea hazy in the lower half, the pupil dilated, the anterior chamber shallow. The tension was about +3. A view of the disc was impossible on account of the hazy cornea. There was no light perception. Patient also stated that he had refused operation recommended by one of the oculists previously seen. His attitude was rather extreme since he said he preferred to be blind to having an operation on his eye.

This course of reasoning followed: This man's right eye is totally blind. He has nothing to lose since he refuses the most probable method of recovering sight. Why not try radium? No harm can be done by the cautious use of radium. If there is any recovery of vision, the patient will have gained, and a new agent will be available for the treatment of glaucoma. The radium was applied to the right eye for one hour. Not

*Reprinted by permission from the Boston Medical and Surgical Journal, etc, 1124-1126, June 26, 1924.

having absolute confidence in radium, the patient was given Eserin and Dionin for local use. He was advised to limit his liquids, use hot applications and take frequent large doses of epsom salts.

The patient returned on April 30 and the vision of the right eye was 20/50 normal; tension +2. Radium was applied for one hour and the patient was advised to continue the treatment outlined above.

The patient returned on May 5th and the vision of the right eye was 20/30 normal; tension +2. Treatment continued. Radium applied.

The vision of the patient on June 8 was 20/50 normal, improved to 20/30+2 with a correcting lens, (+.50 Sph. +.50 Cyl. Axis 90)

Aug. 28, V. O. D. 20/50-1, radium applied.

Oct. 9, V. O. D. 20/50+2, radium applied.

Dec. 11, V. O. D. 20/100, improved to 20/50 with a correcting lens (+.50 Sph. +.50 Cyl. Axis 90). Radium applied.

Jan. 25, V. O. D. 20/70. On this date, tension was taken by McLean Tonometer and registered 40. The patient at all times has kept up the local eye treatment, and it will be noted from the above records of vision that as the interval increased between the dates of application of radium, that there was a tendency of his vision to diminish. This would tend to emphasize the importance of radium in the treatment of this case.

2. J. W., male, 46 years, appeared at the Eye, Out-Patient Department of the Boston City Hospital on Monday, June 4. The patient stated that after boarding the New York train on Saturday night, June 2, he felt a pain in the right eye and the vision began to disappear. When he reached Boston on the next morning, he had to be taken in a taxi to the home of friends because of loss of vision.

Examination showed the patient's right eye to be markedly injected, the anterior chamber shallow, the pupil dilated, and the tension increased to about +3. The cornea was hazy. It was impossible to see the optic disc. The patient could count fingers at one foot. Radium was applied to the right eye for one-half hour and no other treatment was prescribed.

The patient returned on June 6th and the vision was 5/200. Radium was again applied, at this time for one hour.

On June 7th, haziness of the cornea clearing, eye getting softer, tension about +2, pupil still dilated, eye still red, vision 20/70 normal. Patient was anxious to return to New York and in order to speed his recovery, Dionin and Eserin were prescribed with hot applications.

June 9th, the vision was 20/70 normal, tension about +2, pupil still dilated, eye still red. 50 milligrams of radium applied for one hour.

June 11th, cornea clear, disc showed cupping, tension +1, pupil still dilated, injection of globe subsiding, vision of the right eye 20/50 normal, improved with a correcting lens, (-.50 Cyl. Axis 180) to 20/30 normal. The patient left the office in a happy state of mind and naturally very much pleased with the recovery of his vision.

He returned the next day stating that the pain had returned on the previous night. After some interrogation, it was learned that the patient

had taken an automobile ride after leaving the office on the day before. Vision of the right reduced to 10/200, eye markedly injected.

The sudden disappearance of the vision after the automobile ride has become more significant since emphasized by an experience with the condition described in case three. It is probable that the exposure of the eye during the ride precipitated another attack of his glaucoma.

The patient received a telegram from his wife to return to New York immediately. He was advised to consult an oculist at once. Several attempts were made to trace the patient through relatives in Boston. Finally it was learned that the patient had been operated on by a New York surgeon and operation was followed by intra-ocular hemorrhage. Judging from the description received over the telephone, the patient probably has light perception only.

3. A. C., male, 59 years old.

History: Pain in left eye four years ago with failing vision. Consulted a reputable oculist in Boston several months after the onset. Operation was advised and refused. After the consultation, the patient noticed a halo of colors surrounding the lights and continued to lose his vision, until, finally, the left eye became totally blind.

Two years ago, noticed circles in front of the right eye. Eye got red and the pain was more severe. Started treatment under Christian Scientist as soon as the right eye began to bother.

The vision in the right eye had been gradually failing until Dec. 23, at which time the patient had a severe attack of pain and a sudden loss of vision. On Christmas day, the patient stated he could not see the food on his plate.

The patient came to the Boston City Hospital on Jan. 4th, 1924, led by his wife because of his inability to see. Examination revealed the following: Right eye hard and red, cornea hazy, pupil dilated, anterior chamber shallow, view of the fundus impossible on account of hazy cornea. Tension by McLean Tonometer, 100. Light perception. Left eye hard and red, cornea so hazy that it appeared infiltrated, pupil dilated, anterior chamber shallow, view of the fundus impossible, no light perception, tension by McLean Tonometer, 100.

In the two cases previously described, at some time in the course of the treatment, myotics were used, so that they could not be considered purely cases of unmixed radium treatment.

The treatment of this case was started with radium alone. Fifty milligrams of radium were applied for one hour to the right eye, and 100 milligrams of radium for one hour to the left eye.

The Intern was advised to take tension at intervals of two hours on the day of the application of radium and until three records had been made. There was no variation in the tension of either eye.

On the next day, the patient returned to have his tension taken. The right eye showed a tension of 80 and the left eye a tension of 74. The tension was taken again two days later and found to be 65 in the right eye and 70 in the left eye. On this date, radium was again applied to both eyes.

On January 7th, the cornea of the right eye was clear, the cornea

of the left eye showed infiltration. Vision of the right eye, fingers at one foot. Radium was again applied for one hour.

On Jan. 11th, the vision of the right eye was 20/60, improved with a correcting lens, (+.50 Cyl. Axis 180) to 20/40+3. It was now possible to see a thin linear scar extending from 7 o'clock to the center of the cornea. There was also a slight thickening of the anterior capsule of the lens and a more dense area near the lower margin of the lens. Up to this date, nothing had been used in the right eye locally, nor was there any general treatment for the patient's condition.

He was treated with radium and radium alone. His vision had been improved in one week from light perception to 20/60 normal, and, with a correcting lens, to 20/40 normal.

On Jan. 14th, which was a very cold day, the patient walked a distance of two or three miles to the hospital. There was marked epiphora but no pain. The vision was reduced to 20/100 normal. Radium was again applied.

When the patient returned to the hospital again, Jan. 18th, the vision was still 20/100, tension of the right eye 75, the left eye 80.

On Jan. 28th, the vision of the right eye was 10/200 normal and the tension 90. The patient was admitted to the hospital and myotics started. He has been kept under observation and his vision brought back to 20/100 normal in the right eye and the tension to 85.

It has been observed since he has been in the hospital that a dose of 100 milligram hours gives relief for about five days when there is a return of pain, a decrease in vision, and an increase in tension.

The above cases were reported at the meeting of the New England Ophthalmological Society on Tuesday evening, Feb. 19, 1924. Cases one and three were shown and case two simply reported. These cases were shown with the idea of demonstrating that radium is an agent which can be used to reduce intra-ocular tension.

It should not be inferred that radium is considered a panacea in the treatment of glaucoma, that it is the sole agent to be used in the treatment of glaucoma, or that it is to be used as a substitute for myotics or operation. These cases show very definitely that radium will reduce the intra-ocular tension in glaucoma, and incidentally may improve the vision.

After a thorough search of the literature, it was found that the only instance in which radium was used in the treatment of glaucoma was reported by Wickham and Degrais in their book on "Radium Therapy."*

In the latter part of December, 1906, a patient suffering from glaucoma, at the hospital of St. Jean De Dieu at St. Barthelemy, near Marseilles, was sent to Wickham and Degrais in Paris for radium therapy relative to glaucoma. The description of the case follows:

"We have ourselves tried it in a case of glaucoma, which we quote here, not because of the result obtained, which was in no way remarkable, but because of the technique. . . The patient was completely blind in the left eye, and partially blind in the right eye. The eye on this side could distinguish some shadows. The diagnosis of the ophthalmologist at the institution was 'inoperable glaucoma,' of several years' standing."

*From "Radium Therapy" by Wickham and Degrais (Funk & Wagnalls), part iii, chapter ix, pp. 277-278

Notice how in detail, the description of this case corresponds to the condition of the case described in case three.

Quoting further:

"The treatment, commenced on January 23rd, 1907, was repeated every day until February 5th, inclusive. . . . The patient returned to Marseilles on February 12th. During the course of treatment he seemed to see unaccustomed lights, and felt much encouraged. On March 26th M. deM—— wrote to us that there seemed to be improvement; but since then the patient's condition has become the same as before treatment. We give this instance only because it marks our first attempt at filtering radium rays through a lead sheet."

It will be seen that the authors describe the above case primarily to demonstrate the technique which would enable them to use radium in deep therapy, and which, in so far as they knew, had never before been used. Their report on the case mentioned in no way, nor even suggested that radium produced a reduction in the intra-ocular tension; nor did it make, in any way, any definite record of improvement in vision.

The amount of radium element used was 26.8 milligrams, and the time of application twenty minutes daily for fourteen consecutive days. Their method of application was such as to have the benefit of cross-firing.

This dosage is comparatively small both from the point of view of the individual dose and the aggregate. Each separate dose was 8.9 milligram hour and the total dosage for the entire treatment was 124.6 milligram hours. Probably this is wherein the treatment failed.

If the optic nerve had gone on to atrophy, radium or any other element could not be expected to restore its function. When eyes have been glaucomatous for over one or two years, totally or almost totally blind for a period varying from two to fifteen days, and the vision can be brought back, even temporarily, who knows when the optic nerve begins to atrophy and to what degree it is atrophied in these cases of glaucoma?

In so far as can be determined by a study of the literature to date, the cases of glaucoma above described by the writer, afford the only instances and the first records of a reduction of intra-ocular pressure with an improvement of vision by the use of radium.

When an agent of this kind can bring the vision of an eye from total blindness to 20/70 normal in four days as in case one; and when the vision of an eye can be improved from what is practically total blindness to 20/60 normal in seven days by radium alone, then this agent is certainly a factor to be reckoned with and given due consideration in the treatment of glaucoma.

In case one, the patient had been under the care of trained men who undoubtedly gave all the help possible by the use of myotics. It is reasonable to assume that the Eserin and Dionin prescribed on the day that the radium was applied, added nothing to the drug action which had previously been prescribed by the other men. It points very forcibly to the fact that the snap-back in the patient's vision must have been due to something which had not previously been received in the way of treatment.

There is no desire on the part of the writer to convey the idea that radium is the last and only word in the treatment of a glaucoma, but it

must be admitted that it has the power to produce this all important effect, namely, the lowering of intra-ocular tension. There is still much to be learned as to how radium acts, how extensive and permanent its results.

Another very important phase of the subject to be worked out is dosage. It is very necessary to determine whether the best results will be obtained by large doses given at longer intervals, or small doses given at frequent intervals. The impression from observations thus far leads the writer to believe that there is more good to be obtained from one large dose than from several small doses. In treating this condition, the alpha and beta rays should be screened with brass and hard rubber, and the radium placed 2 cm. from the eye, this screening making available the gamma rays without any danger of burning.

It is not unreasonable to assume that radium will become a valuable pre-operative adjunct to the treatment used by the Ophthalmic Surgeon when he desires to lower the intra-ocular tension in cases of glaucoma, previous to operation. Instead of resorting to paracentesis of the cornea or sclerotomy, he may, by the use of radium, be able to lower the tension sufficiently to render his operative procedure safe.

CONCLUSIONS

That in some cases of glaucoma, radium definitely lowers the intra-ocular tension, and this lowering of intra-ocular tension is sometimes accompanied by an improvement in vision.

That the action of radium on intra-ocular tension in glaucoma, suggests a field for worth-while investigation.

1

Roentgen-Ray Treatment of the Spine in Lichen Planus

Ames

J. R. DRIVER, M.D.
CLEVELAND

Reprinted from the Archives of Dermatology and Syphilology
April, 1929, Vol. 19, pp. 620-637

COPYRIGHT, 1929
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO

ROENTGEN-RAY TREATMENT OF THE SPINE IN LICHEN PLANUS

J. R. DRIVER, M.D.

CLEVELAND

Irradiation has been employed in the treatment of dermatoses for many years. The indirect action of x-rays through nerve centers in the treatment of diseases of the skin, however, is comparatively new. Yet, the treatment of lichen planus by irradiation of the spinal cord and the sympathetic ganglions has developed many enthusiastic supporters in France. Moreover, it has opened new fields for investigation and has stimulated considerable discussion regarding the possible neurologic origin of many dermatoses of unknown genesis.

Concerning few diseases of the skin of unexplained etiology are there so many facts that seem to indicate a definite localization of the cause as there are concerning lichen planus. That the nervous system and, more especially, the sympathetic centers play an important rôle in its pathogenesis is suggested by the frequent occurrence of the disease in neurotic persons, often following extreme worry, violent emotions or mental fatigue. The association of marked pruritus, headache and insomnia, the occasional zonal and symmetrical distribution of the lesions and the residual pigmentation after a cure are strongly indicative of nervous etiology. The observations of Thibierge and Ravaut,¹ of Pernet² and of Pautrier,³ that in certain cases of acute generalized lichen planus, withdrawal of from 8 to 10 cc. of spinal fluid will cause the itching to disappear and the lesions to involute rapidly, strengthen this point of view. Certainly, in many cases of lichen planus the intervention of a psychic coefficient acts as a predisposing or determining factor, while in others it is absent.

REVIEW OF THE LITERATURE

Proceeding from such deductions and working independently, Pautrier,⁴ Hufschmidt⁵ and Gouin⁶ began experimentally to treat

* From the Department of Dermatology and Syphilology of the Western Reserve University School of Medicine and of the Lakeside Hospital.

* Read before the Section on Dermatology and Syphilology, Seventy-Ninth Annual Session of the American Medical Association, Minneapolis, June 13, 1928.

1. Ravaut, P.: *Bull. Soc. franç. de dermat. et syph.* **34**:567, 1927.

2. Pernet, G.: *Proc. Roy. Soc. Med.* **11**:81, 1918; *abstr. J. Cutan. Dis.* **37**:156, 1919.

3. Pautrier, L. M.: *Bull. Soc. franç. de dermat. et syph.* **34**:571, 1927.

4. Pautrier, L. M.: *Bull. Soc. franç. de dermat. et syph.* **31**:67, 1924.

5. Hufschmidt: *Bull. Soc. franç. de dermat. et syph.* **31**:71, 1924.

6. Gouin, J.: *Bull. méd.* **38**:1015, 1924.

patients with lichen planus by the administration of x-ray treatment to the region of the spinal cord. Pautrier reported his first success in March, 1924; Hufschmidt in May, 1924, and Gouin, who states that he first tried the method in 1919, made his first report in September, 1924.

Two procedures that differ considerably in character are in vogue. The method used by Pautrier and Hufschmidt, called "the semideep method," consists of dividing the spinal column into five fields, from the first dorsal to the fifth lumbar segments. The rays are directed perpendicularly over the spinous processes; a dose of 4 Holtzknecht units (4H) filtered through 5 mm. of aluminum is given to each field, thereby treating the entire vertebral column. Later, the method of cross-fire irradiation, as successfully used by Bordier in the treatment of anterior poliomyelitis, was adopted. This consists of dividing the spinal column from the first dorsal to the fifth lumbar segments into eight fields, four on each side, and with the rays directed at an angle of about 45 degrees from the perpendicular, a dose of 3 Holtzknecht units is given to each field. This method permits of more thorough irradiation of the cord, and Pautrier⁷ states that two failures by the original method were later successful by the cross-fire technic. He reports that in thirty-five cases two thirds of the patients were cured. In thirteen patients, one treatment sufficed, while in nine others a second treatment was necessary to effect a cure.

The second method, as extolled by Gouin,⁸ called "the superficial method," consists of giving a single dose of 5 Holtzknecht units without filter, perpendicularly over the spinous processes of the interscapular region ("principal sympathetic field"). In fifteen patients with generalized lichen planus, one treatment sufficed to effect a cure, while in four additional patients, it was necessary to treat the lower dorsal spine ("accessory cutaneous field") in the same manner in order to clear up resistant lesions on the lower extremities. Gouin does not report any failures in his series. He states that lesions of the mucous membrane of the mouth are likely to be more resistant than the lesions on the skin. Both methods, often with slight modifications, have been used rather extensively in Europe, and particularly in France, with favorable results, in general.

Louste, Lévy-Franckel and Juster⁹ report thirty-two successes and eight failures after the use of a filter of 2 or 3 mm. of aluminum. Twenty-two of these patients received the treatment over the region of

7. Pautrier, L. M.: Bull. Soc. franç. de dermat. et syph. **31**:159, 1924.

8. Gouin, J.: Bull. Soc. franç. de dermat. et syph. **32**:80, 1925.

9. Louste; Lévy-Franckel, A., and Juster, E.: Bull. Soc. franç. de dermat. et syph. **34**:591, 1927.

the medulla oblongata, which resulted in eighteen successes and four failures. It was necessary in some of the patients to repeat the treatment at monthly intervals until three or four treatments had been given, in order to obtain a cure. Eighteen additional patients, treated by the superficial method of Gouin, gave the result of ten cures and eight failures. These results, they believed, indicated the superiority of the filtered x-ray. Neumark and Krynski¹⁰ treated eight patients by the use of a filter of 3 mm. of aluminum, and exposed the interscapular and lumbar areas to a dose varying from 3 to 6 Holtzknecht units. The applications were given perpendicular to the spinous processes. In their experience, it was necessary to repeat the treatments in order to get the best results. They report that three patients were cured and that three showed marked improvement, while in two, with verrucous lichen planus of the legs, improvement was not obtained. They were able to cause involution of lesions of the mouth in some of their patients. In their opinion, the results were satisfactory in general. They believe that patients with an early, recognizable, generalized involvement of the skin are best suited to this mode of treatment. Hudelo and Rabut,¹¹ who used the Gouin technic in twenty cases, state that the relief from itching was rapid and that the action on the eruption was satisfactory in general, while in lichen planus of the mucous membranes the beneficial effect was much slower and uncertain.

Hudelo, Laporte and Kourilsky¹² treated a patient by giving two applications, interscapular and lumbar, with a dose of 3 Holtzknecht units, filtered through 10 mm. of aluminum. The treatment was then repeated at the end of three weeks, and two weeks later the patient developed a severe, generalized lichen planus which rapidly involuted; the patient was cured in a few weeks without further therapy. Similar transient exacerbation of the disease following roentgenotherapy to the spine has been noted also by Hufschmidt,⁴ Pautrier,¹¹ Gougerot and Filliol,¹³ Roederer,¹⁴ Gawalowski¹⁵ and others. Cottenot¹⁶ has had good results in several patients with lichen planus of the body, but

10. Neumark, S., and Krynski, A.: *Strahlentherapie* **25**:427-442, 1927.

11. Hudelo, L., and Rabut, R.: *Bull. Soc. franç. de dermat. et syph.* **34**:540, 1927.

12. Hudelo, L.; Laporte, and Kourilsky, K.: *Bull. Soc. franç. de dermat. et syph.* **32**:6, 1925.

13. Gougerot, H., and Filliol: *Bull. Soc. franç. de dermat. et syph.* **33**:191, 1926.

14. Roederer, M. J.: *Bull. Soc. franç. de dermat. et syph.* **33**:232, 1926.

15. Gawalowski, K.: *Bull. Soc. franç. de dermat. et syph.* **34**:594, 1927.

16. Cottenot, P.: *J. de méd. de Paris* **39**:795, 1922; abstr. *Dermat. Wehnschr.* **49** and **50**:1458, 1923.

believes that repeated, small filtered doses are as efficacious as the larger doses used by others, and that the danger of acute generalization of the disease is lessened. Sabouraud¹⁷ has never seen patients with lichen planus of the mouth benefited by this new method of treatment, but states that in cases presenting lesions on the skin the results, in general, are excellent. Noguer-Moré,¹⁸ after using Gouin's unfiltered technic in twenty-two patients, reports that the disappearance of the eruption in all cases was extremely slow, although in six instances it was definite. He noted an increase in the itching, often following shortly after the treatment, but in none was there an exacerbation of the eruption. Ramel¹⁹ used Gouin's method in seven cases and reported "excellent results" in two; in three, the itching disappeared quickly but involution of the lesions was incomplete; in one, an exacerbation of the eruption occurred; and in one, influence was not noted. Jeanselme and Burnier,²⁰ using Gouin's method, cured or improved the condition in eight of nine patients with generalized and localized lichen planus, while in five other patients with verrucous lesions, or involvement of the mucous membranes, they did not obtain success. Payenneville²¹ treated four patients with the "semideep method" of Pautrier. In three of these, the eruption was generalized and included lesions in the mouth. All patients were cured in from fifteen to forty-five days following a transient exacerbation of the eruptions. One patient with lesions in the mouth alone was uninfluenced after four treatments. Two more patients treated by the "superficial method" showed a slow, moderate improvement. Payenneville concludes that irradiation of the spine by Pautrier's method gives results superior to all other forms of therapy. In a favorable report made by Gawalowski,¹⁵ he said the itching diminished or disappeared after a short exacerbation. The lesions then involuted, usually in from ten to fourteen days after the treatment. In some instances from two to four treatments were necessary. In one patient, after treatment of the lumbar region only, the lesions on the legs disappeared while those on the arms were uninfluenced. There were two failures by the method. Brocq²² states that by both the filtered and the unfiltered methods the curative action in many cases is remarkable.

17. Sabouraud, R.: Bull. Soc. franç. de dermat. et syph. **33**:192, 1926.

18. Noguer-Moré, in discussion on Pautrier, L. M.: Bull. Soc. franç. de dermat. et syph. **34**:602, 1927.

19. Ramel, in discussion on Pautrier (footnote 18).

20. Jeanselme, E., and Burnier: Bull. Soc. franç. de dermat. et syph. **34**:538, 1927.

21. Payenneville, J., and Billiard: Bull. Soc. franç. de dermat. et syph. **34**:598, 1927.

22. Brocq, L.: Bull. Soc. franç. de dermat. et syph. **34**:507, 1927.

EFFECT OF ROENTGEN-RAY TREATMENT OF THE SPINE
ON OTHER DERMATOSES

Stimulated by the results obtained in the treatment of lichen planus, several investigators have treated patients with various dermatoses by irradiation of the spinal column.

Gouin, Bienvenue and Dewing²³ report on the treatment of 150 patients with various dermatoses by unfiltered irradiation of the sympathetic areas. Excellent results were obtained in the following conditions: erythema multiforme, parapsoriasis, prurigo nodularis and prurigo of Hebra. Similar results, with the use of filtered irradiations, were obtained in pruriginous eczema of the genitalia in women, and in dysmenorrhea and amenorrhea. Varying success was noted in herpes zoster, diffuse neurodermite, urticaria, asthma with cutaneous lesions, and in exophthalmic goiter. Patients with psoriasis, lichen simplex, pelada and dermatitis herpetiformis did not seem to be influenced. They conclude that in numerous patients, in whom pruritus is present, the action of this therapy in relieving the itching will result in a rapid regression of the cutaneous lesions.

Zimmern, Cottenot and Dariaux²⁴ obtained good results in cases of neurodermite. Cottenot²⁵ states that good effects were also obtained in patients with pruritus vulvae et ani and in lichen simplex. Relief from itching was noted in patients with mycosis fungoides.

Kriser²⁶ used a filter of 3 mm. of zinc and obtained a disappearance of itching and an objective improvement in patients with senile pruritus, generalized eczema and psoriasis.

Gawalowski¹⁵ used the method of Gouin and records partial success on some patients with eczema and neurodermite, in whom the itching was relieved and in whom the hyperkeratosis of neurodermite disappeared. He was unsuccessful when patients with psoriasis, hyperhidrosis, urticaria and exfoliative dermatitis were treated by the method.

Good results have also been reported in the treatment of patients with bronchial asthma by Klewitz²⁷ and of those with thrombo-angiitis obliterans by Philips and Tunick.²⁸

23. Gouin, J.; Bienvenue, A., and Dewing, W.: Bull. Soc. franç. de dermat. et syph. **34**:124, 1927.

24. Zimmern, A.; Cottenot, P., and Dariaux: Presse méd. **30**:85, 1922.

25. Cottenot, P.: J. de méd. de Paris **39**:795, 1923; abstr., Dermat. Wchnschr **49**: and **50**:1458, 1923.

26. Kriser, A.: Wien. klin. Wchnschr. **21**:569, 1925.

27. Klewitz, F.: München. med. Wchnschr. **69**:305, 1922.

28. Philips, H. B., and Tunick, I. S.: Roentgen-Ray Therapy of Thrombo-Angiitis Obliterans, J. A. M. A. **84**:1469 (May 16) 1925.

METHOD OF ACTION

The mode of action of this indirect method of treating lichen planus has stimulated considerable theoretical discussion. Pautrier²⁹ sees in its striking and unquestioned curative effect a selective action on the nervous system, but it is impossible at the present time to explain the precise mechanism. Gouin⁸ believes that his method of superficial irradiation of the upper dorsal spine acts on the neurovegetative system by producing a sensitization of the entire sympathetic system, for, he contends, how otherwise could a single exposure affect an eruption generalized in distribution? He questions the rationale of the cross-fire filtered treatment of the spinal cord recommended by Pautrier and Hufschmidt, since, in his opinion, equally satisfactory results are obtained by his simpler superficial method. He believes that the mode of action is identical in both methods. Gouin admits that his reasoning is theoretical but believes that this hypothesis is plausible. Gawalow-ski¹⁵ reasons that since the same results are obtained by both methods, the action could not be on the spinal cord or the sympathetic ganglions, which lie at an equal or greater depth, for these structures would not be affected by the superficial exposure. He thinks that the action is probably a direct one on the sympathetic fibers, which results in a change from abnormal to normal function. Neumark and Krynski¹⁰ suggest that superficial or deep irradiation probably has an influence on the terminal branches of the sympathetic and sensory nerves, which produces a reflex action on the spinal cord and the sympathetic ganglions. Prieto³⁰ assumes that roentgenotherapy in lichen planus acts exclusively on the skin, independently of the region irradiated. He treated several patients by exposures over the skin of the abdomen and in some, involution of lesions on other parts of the body resulted. This view, however, is not held by other investigators who have tried to verify these results. Until the meager knowledge of the functional relations of tissue and nerve is considerably enlarged, I believe that further explanation cannot be made of this interesting phenomenon.

EXPERIMENTAL WORK

Having followed with considerable interest numerous favorable reports by the French dermatologists who have used this new type of therapy, I decided to treat a series of patients who had unquestioned, typical lichen planus. In some, I used the superficial unfiltered irradiation, while in others I employed the more profound filtered method, in order to determine, if possible, the comparative value of each.

29. Pautrier, L. M.: Bull. Soc. franç. de dermat. et syph. **34**:602, 1927.

30. Prieto, G. P.: Bull. Soc. franç. de dermat. et syph. **34**:599, 1927.

The x-ray dosage was computed according to the formula for determining the "standard erythema dose" as developed by MacKee, Remer and Witherbee,³¹ which has been used as a standard in the treatment of various dermatoses by American dermatologists since 1916.

The apparatus used was an interrupterless, high tension transformer with a high tension rectifier, equipped with a point spark gap, an auto-transformer control, a voltmeter and two milliameters. The Coolidge tube filament current was from a step down transformer which was controlled by a choke coil.

Technic.—1. Superficial Unfiltered Method: Two midline exposures with the rays directed vertically were made, one interscapular at about the level of the second dorsal vertebra and the other dorsolumbar at the level of the second lumbar segment. The dosage has varied between one half and five eighths of a standard erythema dose. The factors were 5 milliamperes; 6 inch spark gap (100 kilovolts); 10 inches anticathode skin distance. The time required for the one-half erythema dose was fifty-seven seconds; for the five-eighth erythema dose, one minute, twelve seconds.

The number of treatments in each case varied between one and three. The interval between treatments varied between two and four weeks.

2. Filtered Method: The same areas, also the vertical application, are used as in the unfiltered method. The factors were: 5 milliamperes; 7 inch spark gap (113 kilovolts); distance, 10 inches; 3 mm. of aluminum filter. The time required for one-half erythema dose filtered unit equaled five minutes, fifty-three seconds; for five-eighths erythema dose filtered unit it equaled seven minutes, twenty-one seconds. From one to three treatments at intervals of from two to four weeks were used.

This report comprises a study of seventeen patients with conditions typical of generalized and of localized lichen planus, of which seven were treated by the unfiltered method, and six by the filtered method; in four, because of a lack of response, both methods were used.

In order to evaluate the method better, I have not used other local or internal remedies in any of the patients while under observation.

REPORT OF CASES

CASE 1.—J. A., aged 44, a housewife, consulted me on Sept. 15, 1927, complaining of an intensely itchy eruption on the arms and legs. She said that she had always been nervous and that the eruption had appeared shortly after the death of her mother and the serious illness of her father, which were great shocks to her. The examination revealed the characteristic lesions of hypertrophic lichen planus on the flexor surface of the forearms, the dorsum of the feet and the anterior surface of the ankles. The treatment given on September 15 was: irradiation.

31. MacKee, Remer and Witherbee: X-Rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1927, p. 254.

tion of the spine, five-eighths erythema dose, 3 mm. of aluminum filter, applied to two areas, interscapular and dorsolumbar. The itching increased and the lesions became swollen and inflamed for twenty-four hours after treatment. The itching disappeared after four days, and the lesions involuted rapidly and disappeared at the end of two weeks, leaving only a brownish pigmentation. The patient was cured in two weeks after filtered roentgen-ray treatment of the spine.

CASE 2.—E. S., aged 41, a college professor, consulted me on Sept. 23, 1927, complaining of a marked, generalized eruption of the body and the extremities, of six months' duration. He said that, because of additional duties, he had been much overworked and had worried considerably. Examination showed a characteristic generalized, papular lichen planus with lesions confluent on the flexor surfaces of the arms and over the abdomen and the lumbosacral areas and in the popliteal spaces. There was an annular lichen planus of the forearms and a moderate involvement of the buccal mucosa. The treatment given on September 23 was: five-eighths erythema dose, 3 mm. of aluminum filter to the interscapular and dorsolumbar areas. On September 30, following the first treatment, the patient was considerably relieved of the itching and the lesions were paler. On October 7, the itching was renewed, and new lesions appeared on the body. Treatment was given as before: one-half erythema dose. On October 28, the itching had disappeared and the lesions on the body and arms were almost involuted. There had been less effect on the lesions of the legs. The lesions of the buccal mucosa were improved. The treatment was the same: one-half erythema dose. On November 11, all the lesions of the skin had involuted, leaving a brownish pigmentation; the itching had stopped, and the lesions in the mouth were nearly cleared up. On December 8, the lesions in the mouth had disappeared. The patient is now well. He was cured in ten weeks, with three filtered roentgen-ray treatments of the spine.

CASE 3.—J. D., a carpenter, aged 44, was seen on Oct. 20, 1927, complaining of marked itching and a generalized eruption of eight weeks' duration. The examination showed a severe, generalized papular lichen planus with lesions confluent and markedly infiltrated on the hands, which were swollen to such an extent that he could not close them. There were also lesions in the palms, with some involvement of the feet and ankles, with swelling. There was an extensive involvement of the buccal mucosa with a marked plaque infiltration of the dorsum of the tongue; the vermilion borders of the lips were markedly involved. There was a characteristic papular lichen planus of the body. The eruption had received various local applications. The treatment given on October 20 was: irradiation of the spine, one-half erythema dose, 3 mm. of aluminum filter to the interscapular and dorsolumbar areas. For forty-eight hours following this treatment there was a marked exacerbation of the itching. The eruption remained unchanged. One week after treatment the itching had entirely disappeared, except on the ankles, and the edema of the hands and feet was markedly improved. The patient was able to close his hands. The lesions of the mouth were not appreciably affected. On November 11, the same treatment was repeated. The lesions were involuting, without itching. On November 25, the skin lesions were involuted, almost completely, and there was a marked improvement in the lesions of the mouth. On December 9, there was a complete involution of all the skin lesions. The lesions of the mouth, while having shown marked improvement, still persisted. Roentgen-ray treatment, one-half erythema dose, 3 mm. of aluminum filter, was administered to the cervical spine. The dorsum of the tongue still showed a moderate involvement. X-ray treatment, one-half erythema dose, was given locally to the dorsum of the tongue. The patient was last seen on April 3, 1928, and the tongue was

completely well. The lichen planus of the skin had cleared up in six weeks. The lichen planus of the mouth was greatly improved by irradiation of the spine and finally was cured by direct x-ray treatment.

CASE 4.—S. S., a saleswoman, aged 25, consulted me on Oct. 25, 1927, complaining of an itchy, generalized eruption of six months' duration. She said that she had two children to support, was overworked and worried a great deal over family finances. She had had an attack of herpes zoster seven years before examination. The examination showed a characteristic lichen planus with the eruption distributed over the abdomen, the back and the flanks. There was a marked involvement of the flexor surfaces of the arms and the dorsum of the feet; there were scattered lesions on the legs and the thighs. The mouth was not involved. The treatment given on October 25 was: irradiation of the spine, one-half erythema dose, 2 mm. of aluminum filter, interscapular and dorsolumbar application. On November 8, the patient said that on the night following the treatment the itching had been aggravated and that the eruption had become red in appearance. The eruption showed many involuted lesions, especially on the body; some new lesions had developed on the neck, with itching. The second treatment given was: one-fourth erythema dose, 3 mm. of aluminum filter to the interscapular area and one-half erythema dose, unfiltered, to the dorsolumbar field. On December 6, in spite of the involution of many lesions, new papules continued to develop on the breasts and arms. The itching continued. The third treatment given was: one-half erythema dose, unfiltered, to the interscapular and dorsolumbar areas. On Feb. 17, 1928, the patient was unimproved, and new characteristic lesions continued to develop. At this point, roentgen-ray treatment of the spine was discontinued, and I have not been able to follow the case further. Irradiation of the spine, both by unfiltered and filtered methods, failed to improve the condition after nearly four months.

CASE 5.—N. C., aged 56, a grocer, consulted me on Oct. 28, 1927, complaining of an itchy eruption on the arms and legs, of six months' duration. The examination showed a hypertrophic lichen planus fairly extensive on the flexor surface of the arms, and a few lesions on the anterior surface of the legs, with small papular lesions in the popliteal spaces. The treatment given on October 28 was: irradiation of the spine, five-eighths erythema dose, 3 mm. of aluminum filter, to the interscapular and dorsolumbar areas. On November 11, the lesions on the arms had flattened greatly and the itching had disappeared. Neither the itching nor the appearance of the eruption on the legs was influenced. On November 19, the lesions on the arms had involuted almost completely and a marked improvement was noted on the legs. The second treatment was the same as the first. On November 29, the entire eruption had involuted completely, leaving a moderate pigmentation. The patient was cured in four weeks.

CASE 6.—N. R., a housewife, aged 58, was seen on Nov. 9, 1927, complaining of a generalized, itchy eruption of five months' duration. She said that the eruption had developed shortly after she had received the severe shock of the sudden death of a grandchild. She was extremely nervous and was troubled with insomnia. The itching was almost unbearable. Examination showed a generalized, extensive and severe lichen planus, with lesions confluent on the legs, and with edema of the ankles. The mouth was not involved. The treatment given on November 9 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular and dorsolumbar areas. The response in the relief from itching was rapid; the patient was relieved almost completely in three days. On December 7, the lesions on the body and the arms were involuted almost completely. The lesions on the thighs and legs were improved and the itching was moderately

severe on these areas. Roentgen-ray treatment of the spine was again given, the amount being the same as before. On Jan. 5, 1928, the itching had disappeared from all the areas with the exception of the ankles, where the lesions persisted. Between January 5 and March 23, the patient received four x-ray treatments of one-fourth erythema dose, each, which were directly applied to the lesions on the ankles, and resulted in complete involution. A great improvement was obtained from the unfiltered roentgen-ray treatment. The effect on the lesions was slow, and the involvement of the ankles resisted this type of treatment.

CASE 7.—E. S., single, a nurse, aged 25, consulted me on Nov. 11, 1927, because of an intensely itching, generalized eruption of six months' duration. She said that the eruption had developed shortly after the loss of all her money in a business venture, which caused her great worry. Examination revealed an extensive, generalized lichen planus. The treatment given November 11 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular and dorsolumbar regions. There was an increase in the itching for twenty-four hours following treatment. On November 25, improvement was not noted in the eruption, and new lesions continued to develop. The second treatment was given as follows: one-half erythema dose, 3 mm. of aluminum filter to the same areas. On December 2, the eruption was more extensive and the itching was worse. Irradiation of the spine was abandoned, and x-ray treatments of one-fourth erythema dose, unfiltered, were applied directly to the lesions at intervals of ten days, and the eruption completely involuted after five such treatments. The patient became worse after one unfiltered and one filtered roentgen-ray treatment. An ultimate cure was obtained with x-ray treatment applied directly to the lesions.

CASE 8.—F. A., an automobile mechanic, aged 32, was seen on Dec. 2, 1927, complaining of a severe, itchy, generalized eruption of four weeks' duration. He said that he had recently purchased a repair garage and had worried because of the lack of business. Examination showed a generalized, acute lichen planus on the arms, with some annular lesions. The treatment given on December 2 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular and dorsolumbar fields. The itching was aggravated for twenty-four hours after treatment, and the eruption was a brighter red. The itching had disappeared in less than a week, and all the lesions were involuted completely at the end of four weeks. The patient was cured in four weeks by one unfiltered roentgen-ray treatment.

CASE 9.—O. M., a machinist, aged 34, presented himself at the Lakeside Hospital Out-Patient Clinic on Dec. 24, 1927, with a generalized eruption of six weeks' duration. He said that he had been without employment for several months and had worried considerably on this account. Examination showed marked, acute, papular lichen planus on the arms and legs, with additional annular lesions on the legs. There were a few scattered papular lesions on the trunk. Treatment on December 24 consisted of spinal roentgen-ray therapy, of five-eighths erythema dose unfiltered, to the interscapular and dorsolumbar areas. At the end of one week, the itching was markedly relieved and at the end of two weeks it had completely disappeared from the arms and body. The lesions on the arms and body had involuted after three weeks, with only a partial disappearance of those on the legs. On Jan. 21, 1928, a second treatment identical with the first was given which resulted in complete involution of all lesions two weeks later. The patient was cured in seven weeks, following two unfiltered spinal roentgen-ray treatments.

CASE 10.—J. S., a laborer, aged 50, was seen on Jan. 10, 1928, at the outpatient clinic of Lakeside Hospital, with an itchy, generalized, acute lichen planus of six weeks' duration. There was a moderate involvement of the buccal mucosa. The treatment given January 18 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular and dorsolumbar areas. One week later, the itching was greatly relieved, with complete relief on the arms and the upper portion of the body at the end of two weeks. The lesions were involuting, especially on the upper portion of the body. On February 8, a second treatment, identical with the first, was given, which resulted in complete involution of all the lesions of the skin two weeks later; a marked pigmentation remained. The lesions of the mouth showed little improvement. The patient was cured in seven weeks, following two unfiltered roentgen-ray treatments. The lesions of the mouth were uninfluenced.

CASE 11.—O. S., a woman, a school teacher, aged 30, consulted me on Feb. 23, 1928, complaining of an eruption on the buccal mucosa, of two months' duration. Examination revealed an extremely marked lichen planus on the mucous membrane of each cheek. Neither the tongue nor the skin was involved. The treatment given on February 23 was: irradiation of the spine, one-half erythema dose, filtered, to the interscapular area only. Improvement was not apparent on March 22, and a second treatment identical with the first was given. Improvement had not been obtained by April 12. The patient was unimproved after two unfiltered, roentgen-ray treatments.

CASE 12.—G. M., a druggist, aged 31, consulted me on Feb. 27, 1928, complaining of an itching eruption on the arms and legs, of three weeks' duration. He had been greatly overworked for the past few months, had been sleeping poorly and had feared a nervous breakdown. Examination showed an acute, generalized lichen planus of moderate severity. There were many typical papules on the flexor surfaces of the arms and wrists and on the legs. Lesions were sparsely scattered over the abdomen and the back. The treatment given on February 27 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular and dorsolumbar areas. On March 13, the itching was less marked but was still bothersome. The eruption showed a moderate improvement. A second treatment, identical with the first, was given. On April 4, the patient said that relief from the itching had been complete about two weeks after the second treatment. All the lesions involuted with the exception of some on the legs. A third treatment, the same as previous ones, was given on April 27; all the lesions had involuted and had left a moderate amount of brownish pigmentation. The patient was cured in eight weeks. He had received three unfiltered roentgen-ray treatments.

CASE 13.—A. N., a traveling salesman, aged 33, consulted me on March 19, 1928, and complained of a severe, generalized, itching eruption of four weeks' duration. He said that he had been worried for the past several weeks over the ill health of his wife, who had undergone a serious operation. Examination revealed a typical, acute, generalized lichen planus involving the extremities and body, with extensive and confluent lesions over the abdomen and the lumbar region of the back. The treatment given on March 19 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the interscapular areas. Forty-eight hours following this treatment, the itching became worse, and the eruption became inflamed and redder. The itching was relieved immediately following this. On April 3, the itching, while improved, bothered the patient some at night. The eruption showed only a moderate improvement. A second treatment, identical with the first, was given. On April 12, the itching was worse again, and new

lesions appeared on all the areas. On April 21, the condition was about the same, with the lesions uninfluenced. The patient was given a third roentgen-ray treatment: five-eighths erythema dose, 3 mm. of aluminum filter, to the interscapular and dorsolumbar areas. On May 5, the itching had completely disappeared. The eruption was involuted almost completely. On May 22, the eruption was involuted completely and had left a brownish pigmentation. The patient was unimproved after two unfiltered roentgen-ray treatments; he was cured following an additional filtered roentgen-ray treatment. The period of observation was nine weeks.

CASE 14.—A. L., aged 39, an attorney, consulted me on March 8, 1928, and complained of a moderately itchy eruption on the glans penis, of three months' duration. He had had a similar attack two years previously which had been cured by the application of x-ray treatment direct to the lesions. The patient was neurotic and feared that the present eruption was of a syphilitic nature. Examination revealed a characteristic annular lichen planus of the glans penis. Lesions were not present on the body or in the mouth. The treatment given on March 8 was: irradiation of the spine, five-eighths erythema dose, unfiltered, to the lumbosacral area. On April 16, a second treatment, five-eighths erythema dose, 3 mm. of aluminum filter, was applied to the lumbosacral region. On April 15, five weeks following the first treatment, improvement was not noted. The patient was unimproved after one filtered and one unfiltered roentgen-ray treatment of the spine.

CASE 15.—C. D. aged 39, a bakery salesman, consulted me on March 31, 1928, and complained of an extremely itchy, generalized eruption of four weeks' duration. Examination revealed a severe, acute, generalized lichen planus, especially marked on the trunk. Lesions of the mouth were not found. The treatment given on March 31, 1928, was: irradiation of the spine, five-eighths erythema dose, 3 mm. of aluminum filter, applied to the interscapular and lumbodorsal fields. The itching was temporarily aggravated for several hours following the treatment. All the itching had disappeared at the end of one week. The eruption began to involute, and at the end of three weeks all the lesions had disappeared with the exception of those on the legs, which showed only partial improvement. On April 20, a second treatment, identical with the first, was given. On May 4, the eruption had involuted completely, leaving the usual pigmentation. The patient was cured in five weeks, following two applications of filtered roentgen-ray treatment of the spine.

CASE 16.—D. K., aged 40, a housewife, consulted me on March 6, 1928, complaining of an extremely severe, itchy, generalized eruption, of four months' duration. The patient was neurotic, and said that she worried over family affairs. She had been operated on four and one half years before examination for exophthalmic goiter. The examination showed a characteristic generalized lichen planus. The lesions were grouped especially on the flexor surfaces of the arms, over the lower portion of the back and about the ankles. The treatment given on March 6 was: irradiation of the spine, five-eighths erythema dose, unfiltered, applied to the interscapular and the dorsolumbar fields. On March 20, many new lesions were present, and the pruritus was unimproved. A second treatment, identical with the first, was given. On April 3, the patient was unimproved, and new lesions continued to develop. Roentgen-ray treatment of the spine was abandoned at this point, and one-fourth erythema dose, unfiltered, was applied directly to the lesions. On April 17, a marked improvement had taken place. The itching had almost gone, and the lesions were involuting. A second treatment of one-fourth erythema dose, unfiltered, was given directly to the lesions, which remained. Two weeks later, all the lesions had involuted. On May 29,

the residual pigmentation had faded considerably. The patient had not improved following two treatments by unfiltered roentgen-ray treatment of the spine. There was a rapid response and cure following two unfiltered roentgen-ray treatments applied directly to the lesions.

CASE 17.—L. S., aged 42, a housewife, was seen on March 26, 1928, complaining of an itchy eruption on the wrists, arms and legs, of eight months' duration. Examination revealed an extensive, characteristic, hypertrophic lichen planus with lesions the size of a coin on the anterior surface of the legs and the dorsum of the feet. There were similar lesions, smaller in size, on the flexor surfaces of the wrists. The treatment given on March 26 was: irradiation of the spine, five-eighths erythema dose, 3 mm. of aluminum filter, to the interscapular and the dorsolumbar fields. On May 10, the itching was worse, and new papular lesions of lichen planus had developed on the thighs and the abdomen. The former lesions were moderately improved. On May 24, the eruption had not increased in extent. The itching, except on the legs, had disappeared. The lesions on the arms and wrists had involuted almost completely; there was a slight improvement of the lesions on the legs. A second roentgen-ray treatment of the spine was given. On June 8, all the lesions had involuted, with the exception of those on the legs which, while improved, were still resistant. A marked improvement followed two filtered roentgen-ray treatments of the spine.

RESULTS

From a comparative study of the unfiltered and the filtered methods of roentgen-ray treatment of the spine in seventeen patients with generalized and localized lichen planus, I have obtained the following results.

Effect on Itching and Lesions in Generalized Lichen Planus (Twelve Cases).—In seven cases of the acute, generalized type, of from three to eight weeks' duration, all the patients were cured in from five to nine weeks. Four of these were treated by the unfiltered method, which resulted in a disappearance of the itching—in less than one week in one instance (case 8), while in three instances (cases 9, 10 and 12) the itching disappeared much more slowly. In two patients (cases 3 and 15) treated by the filtered method, the relief from itching was prompt, and these patients were cured in six and four weeks, respectively. In one patient (case 13), relief was not obtained from the itching, nor improvement in the eruption after two unfiltered treatments; yet, following an additional treatment by the filtered method, the itching disappeared a week later, and the lesions rapidly involuted.

2. In five cases of chronic generalized lichen planus, of from four to six months' duration, one patient (case 2), who was cured in ten weeks, received three filtered treatments; the relief from the itching and the involution of the lesions were slow. In one patient (case 16), improvement in the lesions was not obtained following two unfiltered treatments, and the itching became more aggravated after the second treatment. This patient was cured by two additional applications of roentgen ray of one-fourth erythema dose, each, unfiltered, applied direct to the lesions. In a similar patient (case 7) who had received one unfiltered

Summary of Case Reports

♀, female; ♂, male.

♀, female; ♂, male.

and one filtered treatment, the improvement of the itching was only transient, and the eruption became ultimately worse with increased itching. Here again, supplementary applications of roentgen ray, of five one-fourth erythema doses, each, unfiltered, applied direct to the lesions produced quick relief and cure. Also, in another patient (case 6); who had received two unfiltered treatments with the disappearance of all the lesions with the exception of those on the legs, the cure was completed by four treatments of one-fourth erythema dose, each, unfiltered, and applied direct to the lesions. In one patient (case 4), following one unfiltered and two filtered treatments, improvement either subjectively or objectively was not noted.

*Effect on Localized Hypertrophic Lichen Planus (Three Cases).—*In three cases of localized hypertrophic lichen planus, prompt relief from the itching was obtained in one (case 1) of eight weeks' duration, and in another (case 5) of six months' duration. Both patients were cured in four weeks following one and two treatments, respectively, by the filtered method. One patient (case 17) showed prompt relief from itching and partial involution of the lesions on the more severely involved legs, following two filtered treatments.

Effect of Lichen Planus on the Mucous Membranes.—Two of the five patients (cases 2 and 10) who showed lesions on the mucous membranes with moderate involvement of the buccal mucosa had complete involution accompanied by the disappearance of the generalized eruption. One patient (case 2) had received three filtered treatments, and one (case 11) had received three unfiltered treatments. Another patient (case 3), in addition to an extensive generalized eruption, showed an intensely marked involvement of the entire buccal mucosa and the tongue with thick plaquelike lesions. Following three filtered treatments, all the lesions disappeared, except a moderate involvement of the dorsum of the tongue which ultimately completely involuted, following one additional roentgen-ray treatment of one-half erythema dose, unfiltered, directly applied to the process. In one patient (case 11), with only a moderate involvement of the buccal mucosa, a change did not occur for eight weeks following two treatments to the interscapular area by the unfiltered method. One patient (case 14), showing annular lichen planus of the glans and reflected foreskin of the penis, remained uninfluenced after one unfiltered treatment and one filtered treatment over the dorsolumbar spine.

COMPLICATIONS

In five patients, of whom four showed generalized involvement, and one localized involvement, a marked exacerbation of the itching with swelling and hyperemia of the lesions was complained of within a few

hours after the first treatment. This lasted from twelve to twenty-four hours, and was followed usually by a rapid improvement or the disappearance of the pruritus and the beginning involution of the lesions. This interesting fact has been noted by all who have used the method, and Pautrier and others believe this to be a true Herxheimer reaction indicating a direct effect on the seat of the disease.

In two instances in which the patients became worse, there was only a moderate exacerbation in the eruption, which was not comparable to the severe generalization of the disease, almost approaching a dermatitis exfoliativa, reported by Hufschmidt, Hudelo and others.

COMMENT

From these results some rather interesting facts should be noted. It will be seen that all of the seven patients with acute generalized lichen planus were cured following roentgen-ray treatment of the spine, four by the superficial unfiltered method, two by the filtered technic, while an additional one was cured by filtered therapy after aggravation by two unfiltered treatments.

In five cases of chronic, generalized involvement there was only one cure by the filtered method. One patient was markedly improved by unfiltered treatment. There was one failure by the unfiltered method and two failures by a combination of the two methods.

In the three patients with the hypertrophic type of lichen planus, there were two cures, and one patient was markedly improved. All had been treated by the filtered method.

In the patients with involvement of the buccal mucosa, three were cured; two by filtered therapy and one by unfiltered therapy, while there was one failure by the unfiltered method. One other patient, with a marked involvement of the tongue, was greatly improved by filtered therapy. A patient with lichen planus of the penis was unimproved after both methods had been tried.

The relief from itching in all the patients cured was, in general, slower by the unfiltered technic. In four of the seven patients unimproved or only partially benefited by irradiation of the spine, cures were obtained by supplementing this treatment with roentgenotherapy applied directly to the lesions. It was my impression that this response to direct treatment was more rapid and required less dosage than one sees in similar cases in which the patients have not been previously treated with spinal roentgenotherapy. This view is also held by Kriser, Langer and others. Langer,³² in a recent article, advises the use of paravertebral irradiation in conjunction with local irradiation of malignant diseases.

32. Langer, Heinz: *Am. J. Roentgenol.* **18**:137, 1927.

Because as yet a much needed universal or international method of computing x-ray dosage is lacking, much confusion results when one attempts to compare results with those reported by others. Especially in this so since the factors employed have varied in one or more details in nearly every report that has been published. The dosages used in this study, however, have been, in general, less than those used elsewhere.

How is one to interpret these facts? While absolute proof is lacking, it would appear that the complete deep irradiation of the spinal cord in its entire length as recommended by Pautrier is not necessary, for, in many cases, complete involution of the disease is seen from only two exposures which affect the cord in only about one half of its length. If it is assumed with Neumark and Krynski that the effect is on the terminal branches of the sympathetic and sensory nerve fibers, causing a reflex action on the spinal cord, the sympathetic centers or both, and resulting in a profound effect on the cause of the disease, one can then explain the results obtained by the smaller doses, both filtered and unfiltered, used in this study. If this is true, perhaps there is another proof in favor of some disturbances of nerve function in certain cases of lichen planus.

CONCLUSIONS

From a study of this small group of seventeen patients with typical lichen planus treated by irradiation of the spine, I believe the following conclusions may be drawn:

1. Twelve of the seventeen cases, or 70.6 per cent, were favorably influenced. Of these, ten, or 59 per cent, showed complete cures. These results compare favorably with those published by the majority of the investigators.
2. Patients with acute generalized lichen planus show the best response to this mode of therapy. The results are unusually constant and, because of its simplicity, the method has many advantages over the more time-consuming one of direct roentgenotherapy.
3. In patients with chronic generalized lichen planus, the effect is much more uncertain; one patient was cured and one was improved out of five in this series, and therefore it can hardly compare with the more constant results obtainable by direct irradiation.
4. Encouraging results in acute and subacute localized hypertrophic lichen planus of the extremities lead me to recommend the method, particularly if failure has resulted from direct roentgenotherapy or the use of other measures.
5. In lichen planus of the mouth, the results are likely to be uncertain. The method is recommended when other measures fail.

6. Concerning the choice of methods, I believe that this study, while lacking sufficient proof, shows that, in general, the filtered method gives more promise of success. The dosage used in this study was somewhat less than that used by most investigators. The number of treatments given is more than that reported by some, and the time required to produce a favorable result has been, as a rule, longer than that reported by Gouin and Pautrier. The method of smaller doses given on two fields only and repeated, if necessary, has the advantage of greater simplicity and avoids the dangers attendant on greater dosage over more surfaces.

7. Further investigations may ultimately produce the ideal technic, and give even better results.

8. Roentgen-ray treatment of the spine is, then, recommended as a procedure of definite proved value in the treatment of lichen planus and is especially indicated in the acute generalized type. It can be recommended in all other types of the disease in which the patients do not respond to other methods of treatment.

1

2

3

61185

THE EFFECT OF RADIATION UPON CILIATED
EPITHELIUM.

LYMAN H. HEINE, M.D.,

BOSTON.



Reprinted from ANNALS OF OTOTOLOGY, RHINOLOGY AND
LARYNGOLOGY, March, 1936.

Vol. 45, No. 1, Page 60

THE EFFECT OF RADIATION UPON CILIATED EPITHELIUM.*

LYMAN H. HINE, M.D.,

BOSTON.

INTRODUCTION.

Various theories have been advanced as to the normal physiology of ciliated epithelium and how the behavior of these cells has been altered by drugs, temperature, and the surrounding atmosphere.

Since Hilding's¹ earliest work uncovered a rich field for research, the literature has been filled with researches upon all phases of this interesting problem.

Cilia, delicate, weak, frail cilia—such is the popular conception of the type of epithelium in which we have placed a large amount of responsibility for the protection of our nasal cavities from disease. That nature is far more kind than to place a really delicate structure in direct fire of the enemy has been lost sight of by all but a few. Proetz,² however, early in his experiments was impressed by the hardness of so delicate an appearing cell. It is hoped that at the conclusion of this paper, all misgivings as to the delicacy of this structure will have been lost, especially when it is realized that single massive dosages of roentgen rays as high as 24 skin erythemas† permit these cells to live.

It was at Dr. Mosher's suggestion that an attempt was made to study the effect of radium upon tissue cultures of ciliated epithelium, hoping to kill the cells at various points in their life cycle, and then by study learn something of their behavior. A number of problems arose and one or two interesting facts revealed themselves. These will be dealt with at the conclusion of this paper.

As we are dealing with another means of altering cell behavior it was thought best that an attempt be made to bring together some of the facts discovered by other workers, and to present them as a

*Read before the Academy of Otolaryngology and Ophthalmology, Cincinnati, Sept., 1935.

From the Mosher Laboratory, Massachusetts Eye and Ear Infirmary.

†Wherever the term erythemas is used, Skin Erythema Doses is implied.



Fig. 1. This section is of the left side of the septum, opposite the side of radium implantation. The epithelium is essentially normal. The cell outlines are distinct. The nuclei are normal in appearance. The cytoplasm is clear. There are a few goblet cells but these are not excessive.

means of leading up to the main question of the paper, which is the reaction of these cells to radiation.

There will follow then a short description of the alterations in behavior produced by extraneous factors, and finally the behavior of these cells when exposed to radiation.

THE EFFECTS OF AIR CURRENTS, TEMPERATURE, AND DRUGS UPON CILIATED EPITHELIUM.

Hilding² was the first to conclude that this type of epithelium was changeable according to circumstances. His experiments whereby he produced goblet cells by merely closing one nostril of a rabbit are well known. With the production of stratified epithelium upon the opposite side, the side receiving the full force of inspired air, he naturally concluded that the exposed parts of the epithelium were the inactive parts, and that the protected parts were the active.

Latta and Schall,⁸ in a most thorough investigation of the histology of these cells, have shown the hyperplastic potentialities of this epithelium as more protection is demanded.

The Effect of Temperature.—Proetz⁵ has shown that ciliary activity is affected by temperature fluctuation. The optimum temperature is approximately 28 degrees. A temperature of 43 degrees killed the cells, whereas all ciliary motion ceased at 7 to 12 degrees C. the activity again returned at 15 degrees.

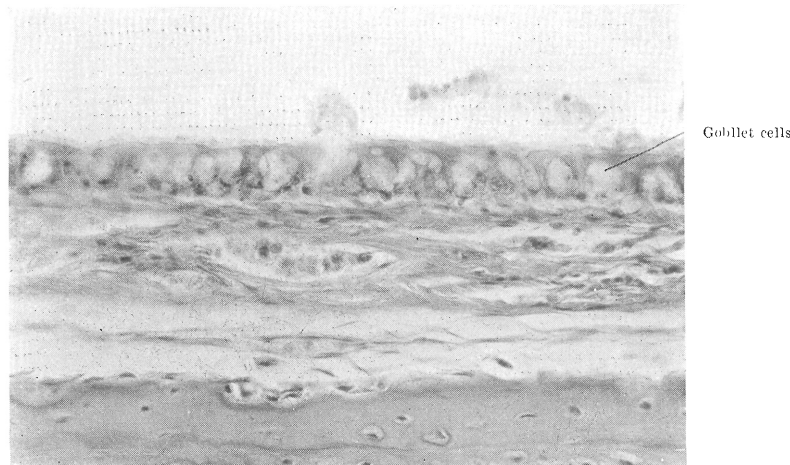


Fig. 2. This section from the same animal is from the right side of the septum. The animal was allowed to live four days following radium implantation. Note the large number of goblet cells. The cell membrane is no longer distinct, the nuclei are pycnotic, and are very indistinct, whereas the cytoplasm of the cell is a little more glandular.

Drying.—Proetz⁶ found further that drying will cause cilia to cease beating, which cannot be restored after fifteen minutes.

The Effects of Solutions and Drugs.—Pursuing his researches further, Proetz³ found that distilled water promptly produces a cloudy appearance to the cilia and the cessation of all motion, whereas solutions of sodium chloride can be increased up to five times the normal before action will cease. This action can be restored again by washing and applying normal saline.

Stark,¹² in studying irrigations of sinuses with sodium chloride noticed that the epithelial cells were larger, that their outlines were less distinct and that the cilia were rarely seen. The goblet cells appeared distended. Studying the effect of mineral oil, ephedrine oil and ephedrine inhalant on the nasal mucous membrane of rabbits, the author found that three out of ten rabbits receiving mineral oil injections showed inflammatory changes, that two out of the same number receiving ephedrine in oil showed inflammatory changes, and one out of the last group receiving ephedrine also showed inflammation. No mention was made of the effect upon the ciliated epithelium except in so far as small fat goblets were noticed in some of the cells.

Proetz⁴ used tissue in situ and excised human material for the study of the effects of various drugs. His basis for studying the effect upon the cell was the vitality of the cells as measured by ciliary movement. His work has been most thorough, and for that reason

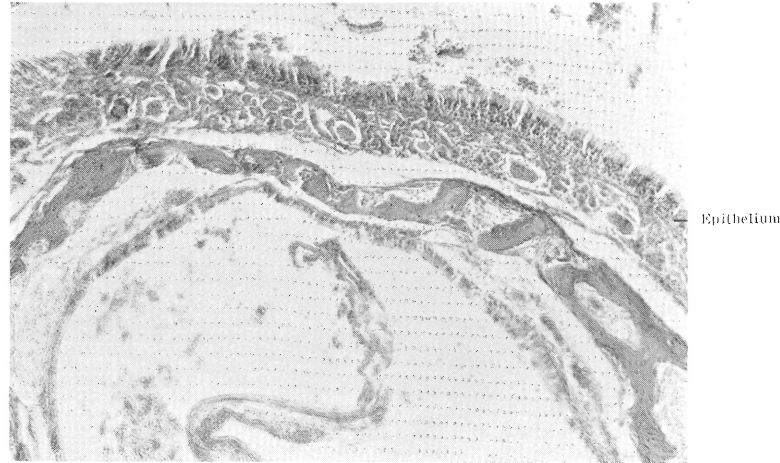


Fig. 3. This section is from the same rabbit and the side exposed to radiation, but was not as near to the radium in that it is from the inferior turbinate. Notice the very high type of epithelium and, judging from the number of cells, it would appear as if the epithelium is hyperplastic.

it is difficult to summarize and still retain all the essential features. Using ephedrine sulphate in 2 per cent and 3 per cent solutions and also in oil, he observed very little effect upon the cilia. Cocain was definitely harmful in strengths above 2.5 per cent, a 10 per cent solution causing ciliary action to cease immediately.

It has been our observation in numerous attempts to produce living cultures from nasal polyps, that if the patient was packed with cocain, no ciliary action could be observed. Frequent washings with Ringer's solution and Locke Ringer's solution failed to revive the activity.

In dilutions of 1/1000 epinephrine likewise caused cessation of the ciliary beat. Dilutions of 1/5000 and 1/10,000 caused slowing of the beat.

Camphor, menthol and thymol in 1 per cent solutions in petrolatum produced but little effect, some irritation being noted from the thymol.

Of the antiseptics, argyrol 10 per cent, mercurochrome 2 per cent, aqueous and dilutions of merthiolate 1/1000 and 1/10,000, the mercurochrome and merthiolate seem to be the most dangerous.

From these observations he concludes that ephedrine is probably not harmful; that cocain or epinephrine should be used in the weakest



Fig. 4. This section corresponds to section III but is from the left side, the side without radium. The epithelium is hyperplastic in this case. However, considerable evidence of infection is present in this specimen, and it may be a hyperplasia for that reason.

solutions; that oily solutions should be avoided; that colloidal solutions should be avoided; that aromatics such as camphor and menthol may be satisfactory, but thymol should certainly be avoided.

Negus¹³ observed the action of chloretone, glycerin and protargol upon ciliary activity. Of the three, chloretone one-half per cent causes paralysis, glycerine 5 per cent produces a retarding effect, protargol in 1 per cent solution produces a harmful effect.

The same author studied the effect of anesthetic vapors and concluded that carbon dioxide and chloroform have but little effect upon the activity of the cilia.

Lierle¹¹ and Moore in further studies have shown that a 2 per cent zinc sulphate and a one-half per cent silver nitrate solution are detrimental to ciliary activity, permanent cessation of activity resulting from the application of the latter drug.

It is difficult to summarize the results of the numerous researches just quoted. Clinical applications can undoubtedly be advanced. However, condemnation of a drug because it shows the activity of the cilia is certainly unwise, for ciliary activity seems to be about the only yardstick that we possess when it becomes necessary to study the effects of various environmental influences upon ciliated epithelium. Suffice it to say that as long as this holds true it would seem that any drug producing a marked defect in that activity should be used with caution.

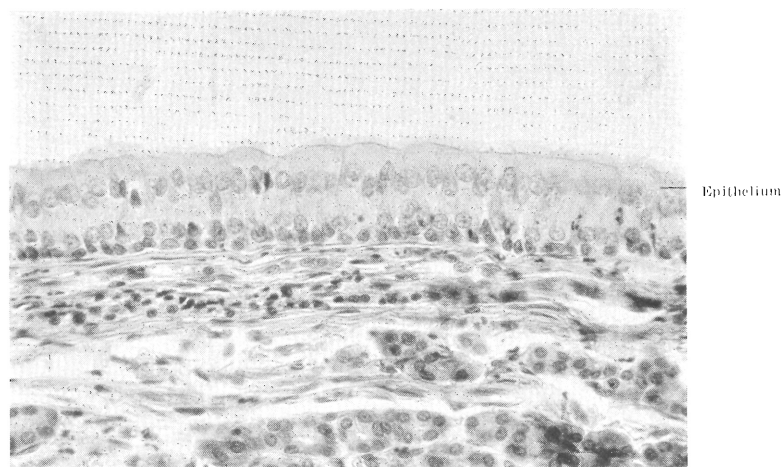


Fig. 5. This is from the unirradiated side of the second rabbit living fifteen days following radium implantation. It is a beautiful example of normal ciliated epithelium from the septum. Cell outlines are distinct, the nuclei are normal, and no hyperplastic changes are noted.

OBSERVATIONS UPON LIVING CILIATED EPITHELIUM FOLLOWING EXPOSURE TO RADIUM AND X-RAY.

Every once in a while during the course of investigation, in some particular field, the original line of thought is interrupted and in its place is substituted some other problem born of interesting observations, while attempting to carry out the primary problem.

The original intention in this case was to study the action of radium upon tissue cultures. However, in the light of subsequent developments the word "cultures" has been dropped and the words "living ciliated epithelium" used. In other words, the following observations are made upon living cells and not the growth of these cells.

Method.

The observations are in reality upon three different types of experiments. These three will be mentioned and the methods used in each case outlined.

Since it was always available, Dr. Mosher suggested the use of tracheal tissue from rabbits. This organ furnished most of the ciliated epithelium except in one case, in the experiment where the cilia beat for eight days. That epithelium was removed from a nasal polyp. Though rigid adherence to sterile technic was not in force, all instruments, glassware and solutions were sterilized.

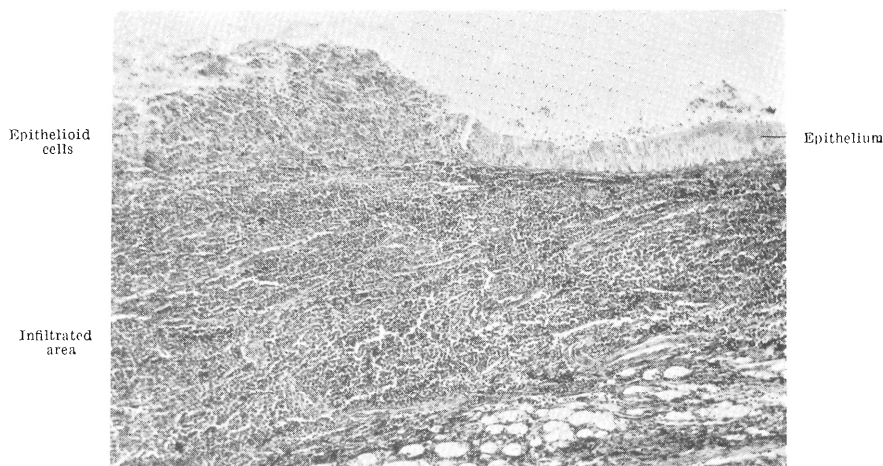


Fig. 6. This is from the radiated side of the rabbit. In this section there is a hyperplasia of the epithelium about an area where the epithelium seems to have been destroyed. Close observation reveals many epithelioid cells, but no order of arrangement and no cellular outline. There is a dense infiltration of lymphocytes.

Pieces of tracheal tissue, one-half mm. in size, were removed and placed in a hanging drop. One mount was used as a control and one was exposed to radium. The tissue was incubated at 28 C. Radon seeds of 1 mc. each were used. These were placed over the cover glass in a circle and were never any more than .5 cm. away from the tissue. The cover glass did not contain lead. The seeds were left in place until the death of the tissue.

The following observations were made:

Shortly after the placing of 6 mc. seeds about the tissue ciliary motion increased. Thereafter it seemed that an increase in ciliary activity was evident with the placing of every dose.

With constant exposure to 6 mc. the tissue lived ninety-six hours. The control lived eight days. Nothing startling was observed, though the growth in both cases seemed to be from the basal layers.

Thirteen attempts at varying the total dosage were tried. However, it soon became apparent that the results were very inconsistent. About the only observation that was made was that very little effect was noted from the radiation. It was then thought that by using x-ray the following factors could be controlled.

1. The dosage could be accurate.

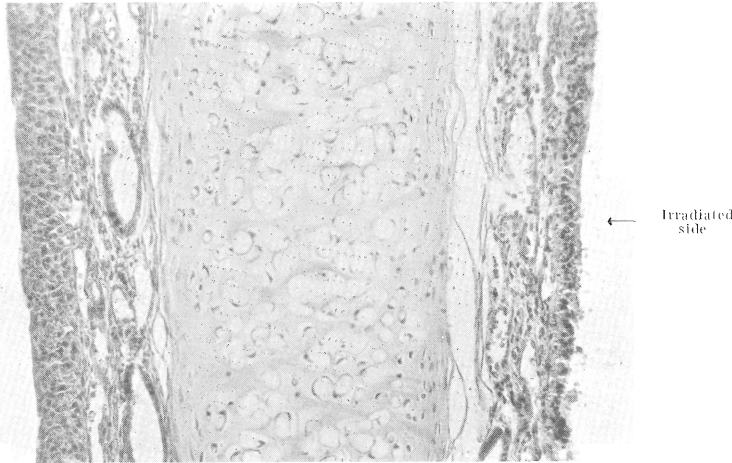


Fig. 7. This section shows both sides of the septum. The animal was allowed to live two months following irradiation. The side opposite the radium shows stratified squamous epithelium, whereas the side of irradiation shows destruction of the epithelium down to the basal layer.

2. The tissue could be exposed directly to the action of the ray.
3. Very high dosage could be obtained.

The following plan of using x-ray was adopted:

After removal of the trachea from the rabbit it was cut into equal portions and each portion washed thoroughly. One specimen was placed in a test tube containing Ringer's solution. The other was laid upon a piece of sterile gauze and kept moist by means of slowly dropping Ringer's solution. This specimen was exposed to the roentgen ray. The rays were not filtered and the target skin distance was eight inches. In all cases single exposures were employed, the machine running at 100 K.V. and 5 M. A.

Following radiation, a small piece of the mucous membrane was removed and placed in the hanging drop. The rest of the tissue was placed in a test tube containing Ringer's solution and kept at a temperature of 14 C. The same was done with the control. From time to time as the hanging drop specimens died, new specimens were made by using the specimens kept at 14 C.

Dosages were started at 4 skin erythema doses, and will be reported in the order of experimentation.

The tissue receiving four S. E. D. lived 120 hours, the control dying at the same time. No visible effects on the ciliated cells were noted, including observations upon the rate of the ciliary beat.

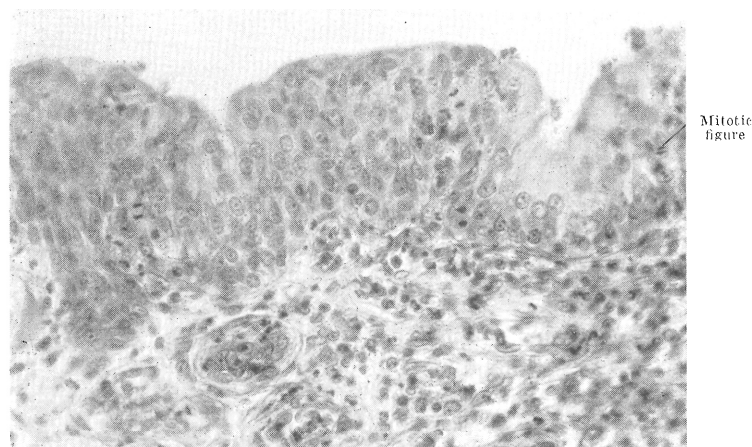


Fig. 8. High power of section of rabbit's nasal mucosa removed from the septum two months following irradiation. The epithelium is markedly hyperplastic. Some degree of its activity may be obtained by the number of mitotic figures present.

Eight erythemas (2800 r).

The tissue lived 168 hours.

The control lived only 48 hours.

Sixteen erythemas (5600 r).

The tissue lived 168 hours.

The control lived 144 hours.

It was thought that at the end of 120 hours, those specimens having received x-ray were a little more active, as measured by the rate and force of the ciliary beat.

Twenty-four erythemas (8400 r).

The specimens which received x-ray lived 314 hours; the control living but 216 hours.

It was observed that after 120 hours, the tissue having received the radiation seemed a little more active and that the amount of debris in the surrounding medium was less than that of the control. By debris is meant dead cells for the most part and leucocytes.

At this point the question arose as to whether or not the metabolism of these cells was being affected. It was decided that some idea of the metabolic rate might be obtained by determining the P.H. of the solutions containing the tissue.

Therefore the experiment of using 24 erythema doses was repeated. This time the exposed tissue lived 168 hours and the control lived 96 hours.

Repeated again, the tissue receiving the radiation lived 192 hours and the control 188 hours.

The P.H. determinations were run up on all solutions and showed so much variation that they were discounted as valueless.

Following this all pyrex glassware was used, the solutions were pipetted and extra controls adopted.

The results were as follows:

Tissue I received 16 erythema doses; lived 192 hours. P.H. of solution 6.2.

Control lived 192 hours. P.H. 6.0.

P.H. of Locke Ringer's solution 7.3.

P.H. of solution subjected to same temperature and conditions as those containing tissue 6.6.

Tissue II received 24 erythema doses; lived 192 hours.

P.H. of solution 6.0.

The control lived 192 hours and had a P.H. of 6.00.

Locke Ringer's solution had a P.H. of 7.3.

The control solution a P.H. of 6.4.

The dosage was now increased to 32 erythemas or 11,200 r. Three sets of tissue were exposed to this increased dosage.

Tissue No. I.

The irradiated tissue lived 48 hours.

The P.H. of the solution was 6.0.

The control lived 96 hours. The P.H. of the solution was 6.0.

The P.H. of Locke Ringer's solution was 6.9.

The control solution had a P.H. of 6.4.

Tissue No. II.

The irradiated tissue lived 96 hours.

The P.H. of the solution was 6.00.

The control lived 168 hours.

The P.H. of the solution was 6.00.

The Locke Ringer's solution had a P.H. of 6.6.

The control solution had a P.H. of 6.3.

Tissue No. III.

The irradiated tissue lived 48 hours.

The P.H. of the solution was 6.00.

The control lived 72 hours.

The P.H. of that solution was 6.00.

The control solution had a P.H. of 6.4.

In general the solutions containing the irradiated tissue and the control had a P.H. of 6.0, the fresh Locke Ringer's solution a P.H. of 7.3 and the control solutions a P.H. of 6.4.

It would seem as if the variation between the control specimens and the irradiated tissues was not enough for any conclusion as to acceleration or retardation of metabolism.

Of considerable interest is the viability of the tissues subjected to the increased dosage of 32 erythemas. The three tissues exposed to this dosage lived 48, 96 and 48 hours, respectively. The controls lived 96, 168 and 72 hours.

From these results it would appear as if an x-ray dosage of 11,200 r was required before any gross effect upon the viability of the ciliated epithelium could be noticed. For the first time during the course of the experiments the control tissue lived longer than the irradiated tissue. In this respect it is of interest to quote the following from Dr. Fenton's¹⁷ paper. "Study of tissues from infected antrum mucosa and cyst walls from a man of 36 who had received doses of deep roentgen rays (because of suspected malignancy) showed enormous thickening and fibrosis of the tunica propria, many plasma cells, and almost normal epithelium."

The third portion of the paper deals with the actual implantation of radon seeds in the nostrils of rabbits. The procedure was carried out along the plan suggested by Dr. Mosher. The same number of seeds was used in each case, the variable being the length of time the animal was allowed to live following exposure.

Five 1 mc. seeds were used. The seeds were partially imbedded in a small mould of dental compound and then inserted in the nostril. The mould was then secured by means of a suture partially closing the nostril. At the end of three days the sutures were removed. In some cases they had sloughed out. It was hoped that in this manner a rather superficial dosage was acquired and that the length of time the nostril was closed would not be sufficient to produce the changes noted by Hilding!²

Section I.

This section is of the left side of the septum, opposite the side of radium implantation.

The epithelium is essentially normal. The cell outlines are distinct. The nuclei are normal in appearance. The cytoplasm is clear. There are a few goblet cells but these are not excessive.

Section II.

This section from the same animal is from the right side of the septum. The animal was allowed to live four days following radium implantation. Note the large number of goblet cells. The cell membrane is no longer distinct, the nuclei are pycnotic and are very indistinct, whereas the cytoplasm of the cell is a little more granular. This section illustrates what I believe to be the early changes resulting from radiation.

Section III.

This section is from the same rabbit and the side exposed to radiation, but was not as near to the radium in that it is from the inferior turbinate. Notice the very high type of epithelium and, judging from the number of cells, it would appear as if the epithelium is hyperplastic. If so, this type of epithelium would correspond somewhat to the type described by Latta and Schall⁸ as being hyperplastic as a means of furthering protection.

Section IV.

This section corresponds to section III but is from the left side, the side without radium. The epithelium is hyperplastic in this case. However, considerable evidence of infection is present in this specimen, and it may be a hyperplasia for that reason. It is unfortunate in that we cannot say that radium produces epithelial hyperplasia as compared to the opposite side. However, the suggestion is certainly present.

Section V.

This is from the unirradiated side of the second rabbit living fifteen days following radium implantation. It is a beautiful example of normal ciliated epithelium from the septum. Cell outlines are distinct, the nuclei are normal, and no hyperplastic changes are noted.

Section VI.

This is from the irradiated side of the rabbit. In this section there is a hyperplasia of the epithelium about an area where the epithelium seems to have been destroyed. Close observation reveals many epithelioid cells, but no order of arrangement and no cellular outline. There is a dense infiltration of lymphocytes.

Section VII.

This section shows both sides of the septum. The animal was allowed to live two months following irradiation. The side opposite

the radium shows stratified squamous epithelium, whereas the side of irradiation shows destruction of the epithelium down to the basal layer. It is quite probable that the radium has made its effect manifest upon the side showing the stratified epithelium, as well as the side devoid of epithelium. Consequently, that side has undergone hyperplastic changes to the point of an absolute change in morphology, whereas the side receiving the full dose of radium has passed through this stage and has entered the stage of destruction.

Section VIII.

This section is from another rabbit allowed to live two months following irradiation. The large number of mitotic figures is an index of the type of activity the epithelium is undergoing.

From these studies it would appear as if ciliated epithelium undergoes the following changes following radiation:

1. Hyperplasia.
2. Loss of cell outline and the production of pycnotic nuclei.
3. Goblet cell formation.
4. Destruction down to the basal layer.

The minute cellular changes produced by x-ray have been thoroughly studied and published in a volume by Colwell.¹⁶ These studies are concerned with types of tissue other than ciliated epithelium.

For the sake of completeness, we are attempting studies upon the mitochondria and Golgi network in ciliated epithelium following exposure to x-ray.

The functions of these two cytoplasmic inclusions are still not definitely known. Many workers, however, contend that the mitochondria have to do with respiration. Therefore, the possibilities of research along this line are rather exciting.

Briefly, we are using a supervital stain of Janus Green B for the mitochondria. The other procedures for fixed specimens are the Bensley-Altman method for mitochondria and DaFano's modification of Cajal's silver impregnation for the Golgi apparatus.

Under supervital staining it would appear as if x-ray produces a clumping and then a vacuolization of the mitochondria, though this observation is awaiting confirmation by the study of fixed specimens.

The work has just been started and no definite conclusions are to be drawn from this stage.

SUMMARY.

The foregoing paper is in two parts. The first deals with some of the outstanding contributions to the literature within the last five years, pertaining to the effects of drugs upon ciliated epithelium.

The second part has recorded observations made upon the behavior of ciliated epithelium after exposure to radiation. Three methods of approach to this problem were used: namely, the exposure of hanging drop specimens of ciliated epithelium to the action of radon seeds; second, the exposure of sections of rabbit's trachea to the direct action of roentgen ray; third, the implantation of a fixed dosage of radium in the nostrils of rabbits and observations upon the histologic specimens made at varying lengths of time after the implantation.

CONCLUSIONS.

1. Goblet cells may be another form of ciliated epithelial cells. Furthermore, they are probably degenerative, as shown by changes noted in the nasal mucosa of rabbits after exposure to radium.

2. The metabolic rate of the cells evidently was not affected by roentgen ray when this metabolic rate was measured by changes in the P.H. of the solutions containing the tissues.

3. It may be possible that some dosages of roentgen ray are actually stimulating. Therefore, there should be a dosage that will produce beneficial results.

4. Ciliated epithelium is not a delicate structure. If one considers that a single dose of unfiltered roentgen ray of eight erythemas is the maximum for the skin of man, the picture of the severity of a burn produced by a single dose three times that amount, or twenty-four erythemas, is almost beyond one's imagination. However, the evidence points toward the fact that these frail appearing cells do stand such a dosage with impunity.

In searching for an answer to the question, "Why are these cells so remarkably viable?" I can find no better explanation than the one offered by Dr. Werner Mueller, namely, that cilia are an ancient structure biologically; that, therefore, in the order of events, they should be the last to be destroyed.

The author wishes to express his sincere thanks to Dr. G. H. Holmes and his staff of the X-ray Department at the Massachusetts General Hospital for the use of their x-ray equipment and radon seeds necessary for the carrying out of these experiments; likewise for such technical advice as was essential for their use. The photomicrographs were taken by Dr. Werner Mueller.

REFERENCES.

1. Hilding, A.: Experimental Surgery of the Nose and Sinuses. *Arch. Otolaryng.*, 16:9 (July), 1932.
2. Hilding, A.: Four Physiologic Defenses of the Upper Part of the Respiratory Tract. *Ann. Int. Med.*, 6:227-234; (Aug.) 1932.
3. Proetz, A. W.: Five Preliminary Notes on Nasal Function. *ANNALS OF OTOTOLOGY, RHINOLOGY AND LARYNGOLOGY*, 41:1117-1123; (Dec.) 1932.
4. Proetz, A. W.: Nasal Ciliated Epithelium with Special Reference to Infection and Treatment. *J. Laryng. and Otol.*, 49:557-569; (Sept.) 1934.
5. Proetz, A. W.: Effect of Temperature on Nasal Cilia. *Arch. Otolaryng.*, 19:607-609; (May) 1934.
6. Proetz, A. W.: Nasal Cilia in Living Mammals. *ANNALS OF OTOTOLOGY, RHINOLOGY AND LARYNGOLOGY*, 42:778-788; (Sept.) 1933.
7. Proetz, A. W.: Effects of Certain Drugs Upon Living Nasal Ciliated Epithelium. *ANNALS OF OTOTOLOGY, RHINOLOGY AND LARYNGOLOGY*, 43:450-463; (June) 1934.
8. Latta, J. S., and Schall, R. F.: Personal Communication—The Histology of the Epithelium of the Paranasal Sinus Under Various Conditions.
9. Lucas, A. M., and Douglas, L. C.: Principles Underlying Ciliary Activity in Respiratory Tract. Comparison of Ciliary Activity Under In-Vitro and in Vivo Conditions. *Proc. Soc. Exper. Biol. and Med.*, 30:501-506; (Jan.) 1933.
10. Knowlton, C. D., and McGregor, G.: How and When the Mucous Membrane of the Maxillary Sinus Regenerates. *Arch. Otolaryng.*, 8:647-657; (Dec.) 1928.
11. McGregor, G.: Further Proof of the Regeneration of Mucous Membrane in the Human Antrum. *Arch. Otolaryng.*, 14:309; (Sept.) 1931.
12. Stark, W. Berkley: Effect of Mineral Oil and Solutions of Ephedrine on the Normal Nasal Mucous Membrane of the Rabbit. *Arch. Otolaryng.*, 16:39-45; (July) 1932.
13. Negus, V. E.: The Action of Cilia and the Effect of Drugs on Their Activity. *J. Laryng. and Otol.*, 49:571-585; (Sept.) 1934.
14. Lierle, D. M., and Moore, P. M.: Effect of Drugs on the Ciliary Activity of Mucosa of Upper Respiratory Tract. *Arch. Otolaryng.*, 19:55-65; (Jan.) 1934.
15. Colwell, Hector: The Method of Action of Radium and X-rays on Living Tissues. Oxford Medical Publication; 1935.
16. Fenton, Ralph A., and Larsell, Olaf: The Histopathology and Clinical Interpretation of Experimental Sinus Disease. *Tr. Am. Acad. of Ophth. and Otolaryng.*, pp. 338-340; 1933.
17. Fenton, Ralph A., and Larsell, Olaf: Report on Research of Experimental Sinusitis; 1934-1935. Read before the American Academy of Ophthalmology and Otolaryngology, Sept., 1935.

2. The second section focuses on the role of technology in modern record-keeping. It highlights how digital tools and software can significantly reduce the risk of human error and streamline the process of data collection and analysis. The author argues that adopting advanced technologies is not just a convenience but a necessity for staying competitive in today's fast-paced market.

3. The third part of the document addresses the challenges of data security and privacy. It notes that as the volume of data increases, the potential for breaches and misuse also grows. Therefore, it is crucial for organizations to invest in strong cybersecurity measures and to establish clear policies regarding data protection. The text also touches upon the legal implications of data handling, reminding readers to stay compliant with relevant regulations.

4. The fourth section discusses the importance of regular audits and reviews. It explains that periodic checks are necessary to verify the accuracy of the records and to identify any discrepancies or areas for improvement. The author suggests that these audits should be conducted by independent parties to ensure objectivity and to provide a clear picture of the organization's current state.

5. The final part of the document provides a summary of the key points and offers some practical advice for implementing the discussed strategies. It encourages organizations to take a proactive approach to record-keeping, viewing it as a continuous process rather than a one-time task. The text concludes by stating that while the initial setup may be challenging, the long-term benefits of a well-maintained record-keeping system are undeniable.

Mechanical and Physical Agents, Special Reference to Radium.

By WILLIAM H. CAMERON, M. D.
Pittsburgh

(Read in the General Meeting of the Medical Society of the State of Pennsylvania, Philadelphia Session, September 23, 1913.)

Reprinted from Pennsylvania Medical Journal, December, 1913

It was my intention to place before you a comparative study of the results obtained in certain conditions treated, first, by ordinary methods and, later, by physical and mechanical measures. Upon assembling my evidence, however, I found that the conditions are scarcely comparative. One working entirely with nonmedicinal measures seldom encounters a case in the acute stage. Time has had an opportunity to alter symptoms, mask the pathology to a greater or less extent, and to increase, or decrease, the tolerance of the patient. Consequently a convincing comparison is not possible when conditions are not parallel. Furthermore, in order to study the value of the many mechanical and physical agents said to possess therapeutic value, it is necessary to have, in addition to the knowledge required for the study of pharmacology, a certain natural mechanical instinct, for it is this ability which must serve in place of properly prescribed technic for the individual case, and I firmly believe it is the lack or the possession of this instinct which gives rise to such a diversity of opinion regarding the true therapeutic value of mechanical and physical agents.

This paper therefore, must deal entirely with personal experience and, being personal evidence, I can not hope to establish true therapeutic values other than by contributory evidence.

To my mind radium is the most valuable physical agent we possess. Considering its rather short period of use for therapeutic purposes, and our present limited knowledge of its true physiological action, this may seem a rather broad statement. An exceptional clinical experience in all forms of radium therapy, access to a well-equipped pathological department devoted entirely to the study of the action of radium on man and animals, and an opportunity to study physical properties in one of the best radium research laboratories in the world, gives me the necessary courage for such a statement.

I have had no personal experience with the use of the x-ray other than for diagnostic purposes but my reason for placing radium above this most valuable physical agent is as follows: Radium when applied locally, when administered by mouth, by inhalation and by intravenous injection gives definite physiological action with demonstrable therapeutic result. Such diversified means of administration can not be had with any other physical or mechanical agent and, I might also add, with any pharmaceutical preparation.

To give an outline of its physical properties, the manner of its preparation for therapeutic purposes and its therapeutic possibilities, would consume the entire time allotted to this paper. Suffice it to say that

Radon

radium, for all practical purposes, is an element which, by reason of its rays, can be used locally for its actinic powers and internally for its physical or chemical effects. The mechanism of this latter process is still a matter of doubt and must be satisfactorily worked out before the true physiological action can be definitely stated.

In the process of disintegration radium produces a gaseous product known as the radium emanation. This gas possesses the property of radioactivity in even a higher degree than radium and is soluble in water. The emanation can be inhaled mixed with air or oxygen and this affords a less expensive way of administering radioactive material internally. It is, of course, understood that the emanation after a certain time loses much of its value and the radioactivity of bath and drinking water containing only emanation, is not permanent, the activity being lost because of the rapid decay of the emanation and its products.

During the past six years, particularly in the last two years, medical literature has contained many articles on the therapeutic value of radium. Most of the articles, dealing with internal administration, are indefinite as to the amount, or rather the dose, of radium used in a given case or group of cases. His claims therapeutic results from five mache units per liter, while in Noorden has given dosage of 35 to 200 mache units. According to the latest report from the Radium Institution of London they have administered 2,500,000 to 3,000,000 mache units per liter in the form of drinking water.

From such diverse opinions it seemed necessary that some effort should be made toward the establishment of a more definite dosage and, to work out this problem, we established at the clinic in Pittsburgh the following arrangement of our emanation inhalation and emanation drinking water treatment.

(At this point I wish to explain that, hereafter, I shall use the terms micro-

millicurie instead of mache units in speaking of emanation dosage, the term mache units having been discarded by most authorities on radioactivity. Bear in mind, then, that one microcurie per liter equals a concentration of about 2700 mache units.)

One twelve-patient room emanator, 2 to 8 milligrams of radium element, 0.003 to 0.025 microcurie per liter.

One two-patient room emanator, 25 milligrams of radium element, 0.7 to 0.8 microcurie per liter.

One two-patient portable emanator, 2.7 milligrams of radium element, 0.1 microcurie per liter.

One twelve-patient room emanator, 50 milligrams of radium element, 0.14 microcurie per liter.

In addition to the above our emanation solutions for the large and small room emanator were so arranged that we were able to use them in combination, thus giving us a wide range in dosage. As a matter of fact our patients had the opportunity to inhale for one and a half hours per day, emanations from 2, 2.7, 8, 25, 50 and finally 75 milligrams of radium element. They were also given one liter per day of emanation drinking water having a concentration of from 0.4 microcurie to 0.6 millicurie.

Provided the patient had equal lung capacity, then we were reasonably sure that we were administering a definite daily amount of radium concentration for stated periods of time. On this information we based the effect of various amounts on different groups or types of cases.

In reading reports of conditions benefited by the internal administration of radium one is impressed by the fact that it must have marked analgesic properties, especially for that low-grade pain associated with certain subacute and chronic conditions of the joints, muscles and nerves. It was natural then, to build up our clinic largely with cases of this type and accepting only such other cases as have proved refractory to other lines of treatment.

Up to and including September 1, 82 cases have been accepted. Of this number 67 were subacute and chronic arthritis, 1

out, 1 inherited ataxia, 2 pseudomuscular hypertrophy, 4 sciatic neuritis, 2 neurasthenia, 2 paralysis, 1 diabetes, 1 chorea, 1 ironic neuritis.

In an effort to arrive at the effect of radium on the various types of arthritis (subacute and chronic) the accompanying classification was adopted. It should be noted that this classification is based entirely on clinical evidence.

These cases were accepted without regard to the local condition of joints, the amount of deformity, the age, the presence of complications, the social condition or the length of time since onset of joint symptoms. The ages of the patients ranged from eight to sixty years and the joint symptoms extended for a period of from six months to thirty years. For a number of months the pulse temperature and blood pressure of each patient was charted before and after each treatment. Blood counts and an analysis of the urine were made at frequent intervals. A few selected patients were bled after having spent one and a half hours in

the emanation room and the blood taken to the laboratory to be examined for radium emanation. Case histories were recorded as carefully as possible and numerous notes taken of the progress made. X-ray plates, photographs, measurements of joint action, weight of patients and other data supplemented the records.

In a paper of this character it is not possible to go into detail and I must briefly report the results as follows:—

No.	Type of Case. (See Classification.)	Not Improved.	Improved.	Cured.	Still under Treatment.	Discontinued during Treatment.*
0—	A. P. I. A.	0	0	0	0	0 (no cases)
5—	S. P. I. A.	0	0	5	0	0
4—	C. P. I. A.	0	0	2	0	2
3—	A. S. I. A.	0	1	0	0	2
14—	S. S. I. A.	1	1	7	2	3
17—	C. S. I. A.	1	2	2	5	7
0—	A. P. I. A.	0	0	0	0	0
3—	S. P. I. A.	0	0	3	0	0
6—	C. P. I. A.	1	1	2	1	1
0—	A. S. I. A.	0	0	0	0	0
2—	S. S. I. A.	0	1	0	0	1
12—	C. S. I. A.	4	2	2	3	1
66		7	8	23	11	17

*Patients not under treatment long enough for any effect.

ACUTE STAGES.

Cases are placed in the acute stage when motion in affected joints is not impaired other than by the acute inflammatory process and where there is a constant temperature curve.

SUBACUTE STAGES.

When the joints can be moved by voluntary or passive motion without causing additional or recurring local inflammatory symptoms or fluctuations in temperature.

CHRONIC STAGES.

When degeneration, or organized exudates, causes fixation and deformity.

OUTLINE OF CLASSIFICATION.

- a. Acute Stage: Acute Articular Rheumatism, Rheumatic Fever.
1. Primary Infectious Arthritis...

- b. Subacute and Chronic: Rheumatoid Arthritis, Chronic Arthritis.

Cases characterized by sudden onset with severe constitutional and joint symptoms. Tendency for complete recovery. In many cases, however, joint conditions never return to normal, the end result being arthritis deformans.

- a. Acute Stage: Rheumatic Fever, Gonorrheal Rheumatism, etc.
2. Secondary Infectious Arthritis...

- b. Subacute and Chronic: Chronic Arthritis, Arthritis Deformans, Degenerative Arthritis.

Mono or polyarticular symptoms coincident with or following a demonstrable acute infection, such as tonsillitis, gonorrhea, syphilis, pneumonia, tuberculosis, etc. Characterized by sudden onset with constitutional symptoms of greater or less intensity and a prolonged subacute stage. Tendency of joint symptoms to become chronic.

3. Primary Toxic Arthritis.....
 - Acute: Difficult to Demonstrate.
 - Subacute: Chronic Arthritis.
 - Chronic: Arthritis Deformans, Polyarthritis, etc.

Coincident with toxin producing conditions such as chronic appendicitis, pyorrhea, etc. Characterized by slow onset with slight general symptoms, and having many acute exacerbations with apparent quiescent periods with gradual tendency to deformity.

4. Secondary Toxic Arthritis.....
 - Acute: Difficult to Demonstrate.
 - Subacute: Chronic Arthritis.
 - Chronic: Arthritis Deformans, Polyarthritis, etc.

Coincident with a toxin producing agent, such as found in what we know as "cultural" metabolism. Characterized by gradual onset, joints affected, never becoming normal, having a long life history, and finally having the end result of deformity.

The word "improved" in this table applied only to joint symptoms and the word "cured" refers to cases in which all joint symptoms disappeared. We do not say permanently cured because of the too recent discharge of the patients.

Of the other conditions treated the case of gout showed marked improvement. The treatment was discontinued and as some of the symptoms returned the patient was given an injection. As to the present condition of this patient I have no knowledge. In the case of inherited ataxia the patient has been under treatment for some months and shows marked improvement. In two cases of pseudomuscular hypertrophy the patients are still under treatment and show little if any improvement. In the four cases of chronic sciatic neuritis the patients have been relieved of considerable pain. Two of them entirely so. The others are still under treatment. The two cases of supposed neurasthenia did not improve under emanation and the patients were given radioactive baths with encouraging results. The two cases of paralysis did not show improvement. In the case of diabetes the patient at first gave remarkable signs of improvement generally and in the urine analysis. Later the per cent. of sugar increased but never up to the percentage in first reports. Still later he developed a severe case of enteritis and discontinued treatment. In the case of chorea the patient was given a few warm radioactive baths which, on account of severe nose bleed, were discontinued. I simply mention this case because hemorrhage is given as a contraindication. In the case of chronic multiple neuritis (diagnosis not positive) the patient was relieved of all pain.

During the course of this clinic some interesting points regarding radium emanation therapy have been observed, and, from our experience, I feel safe in recommending the following dosage: I reserve the right, however, to alter this dosage as further experience demands.

In case such as classed under subacute

primary and secondary infectious arthritis, cases of chronic gout, subacute and chronic neuritis and myositis the patients should have at least one and one half hours daily treatment of a concentration from 0.025 to 0.1 microcurie per liter of air, together with 1 liter per day of emanation drinking water (divided into four doses) of 15 to 20 microcuries per liter.

Cases of subacute primary toxic arthritis are favorably influenced by the above dosage but the treatment must extend over a much longer period of time for final results.

The chronic primary toxic type requires a larger dosage. This may be had by extending the period of inhalation of the above mentioned concentration and increasing the dosage of drinking water. I believe, however, that a concentration of from 10 to 15 milligrams of radium element for two hours per day would be better therapy.

As to the proper dosage for the subacute and chronic secondary toxic type I am not prepared to say as we had about the same results when using the emanation from 25 as from 75 milligrams of radium element. The larger dosage gave us reaction more quickly, but, as I have not as yet experimented with increased time for each inhalation in this type, I will make no recommendation.

Most patients receiving the treatment experience a more or less violent reaction, in that the joints become more tender and swollen, with perhaps a slight rise in temperature. No definite time can be stated when this action should take place. It appeared to depend largely upon the susceptibility of the patient. If no action whatever is noted after sixty days the case is not a favorable one, although in two cases in which no reaction was experienced and the patients discharged, they returned after a period of thirty days and stated that some improvement had been noted. Following up this point, we found that patients with subacute and chronic primary infectious arthritis do better when the treatment is pushed through the reaction period with

no rest until all symptoms have subsided. They should then be treated every other day for a week or ten days before being discharged.

In cases of chronic secondary infectious type, patients should receive one rest day per week.

In cases of toxic type patients probably do better when treated continually for about sixty days, given rest period for six or seven days, and the treatments again pushed.

I believe that, in the case of women who experience an increased flow, all treatment should be discontinued during the menstrual period.

It is noted in most of our blood pressure charts that the emanation treatment has considerable effect on the blood pressure. The curve in cases presenting a high pressure gradually descended. Incidentally these observations led to the use of the intravenous injection of radium element which procedure, I believe, originated at the clinic at Pittsburgh. I am at least sure that this method has never before been conducted on such a large scale as it has in our clinic. Of this I will speak later.

During the early months of the clinic many patients spoke of the somnifacient effect of the treatment and I concluded to substitute the warm and neutral radioactive bath for patients presenting marked nervous symptoms. I also give many such baths to private patients and certainly have found them superior to all other mechanical or physical agents, especially in producing sleep and for relief of indefinite nervous symptoms. That this effect is not due to mental attitude is shown by comparison with many control baths given without radium but with the same technic, temperature of water, etc.

Another interesting feature was testing the blood for radium emanation. These tests show beyond a doubt that the blood becomes highly radioactive under emanation. This work has not, as yet, been taken up in detail. The establishment of a biochemical

laboratory in connection with the clinic will, I hope, clear up many problems not now thoroughly understood.

As our knowledge of joint pathology increases and my knowledge of the clinical effect of radium in certain joint conditions also increases, I most sincerely believe that the future treatment for all types of chronic arthritis (with the exception of the tubercular and syphilitic) will be a preliminary course of radium therapy, then the removal of the infection, if same can be determined, and this followed by additional radium therapy. I make this statement because I have seen all joint symptoms eliminated in spite of active infecting foci.

The second interesting feature of the work has been the development of the intravenous injection of radium element, mainly through the efforts of Dr. Frederick Proescher. For this work we have had placed at our disposal amounts ranging from 5 micrograms to 1 milligram. The various amounts were put up in normal salt solution and sealed in sterilized glass ampules. The largest dose given to a human being was 1 milligram; the next largest $\frac{1}{2}$ milligram, the average dose being from 50 to 100 micrograms. Dr. Proescher and I have worked independently during these experiments, the idea being to compare the clinical and pathological results. As our experiments are not complete I am at liberty to give only a summary of my personal clinical observations. Up to and including September 15, I have given twelve injections to seven patients. Of these, six were cases of arthritis and one a case of recurrent cancer of the breast. In the cases of subacute secondary infectious arthritis the results in four cases were startling in the severity of the reaction and for the rapidity with which all symptoms cleared up. In one case of chronic arthritis, probably complicated by tuberculosis, no result has been noted, and in the last one (chronic secondary toxic arthritis) a slight improvement has been noted. This last patient, I might add, had been previously on

nanation without improvement. The injection given in the recurrent sarcoma case as administered to note the effect, if any, in the cachexia. Unfortunately this case was so situated that it could not be personally followed but the physician in charge informs me that the patient appeared to be much improved generally for some time after its administration. In all the cases the blood pressure was reduced, the red cells increased and the leukocytes first increased and later decreased. The only unusual symptom as noted in one case was the rapid and extensive reduction of the blood pressure and although the patient felt absolutely no discomfort he was given a hypodermic injection of strychnin sulfate, 1/30 grain.

The same effect has been noted, Dr. Proescher informs me, in a majority of the twenty-two patients he has injected.

After an injection the radium has been recovered, to some extent, from the blood and the urine. In experiments on animals it has been recovered from the bone marrow. We conclude then, that a large portion of the radium element injected remains in the system and even if it has been thrown out of solution it will continue the process of disintegration and its therapeutic action. Considering this fact, borrowing from what I know of Dr. Proescher's work and my own personal experience, I venture to put forth the following conclusions:—

Intravenous injections of radium element in doses from 25 to 100 micrograms is perfectly safe and is indicated in all forms of acute, subacute and chronic arthritis not complicated by a heart lesion or advanced arteriosclerosis. (It is evident, of course, that I recommend its use in cases presenting degeneration of joint structure, as a prophylactic measure only.) It should not be administered more frequently than every ten days and is preferably given in increasing doses. The lethal dose has not been determined, but I would not with my present knowledge feel safe to recommend an accumulated dose of over 300 micrograms.

It is to be noted that reduction of blood pressure follows both the administration by inhalation and by intravenous injection. The same can be said of the local applications of large amounts of radium to the rectum and vagina. In such cases I have noted a fall from 115 to 65 during a period of one week; this in a case of cancer of the uterus, 70 to 100 milligrams of radium element being used. In a case of cancer of the rectum practically the same thing was noted with 50 milligrams.

In only one case of exceedingly high blood pressure was an apparent bad effect noted. This case was furnished with 1 liter of drinking water per day (concentration of 20 microcuries) for three or four days. The physician in charge of this case reported that after a preliminary fall the pressure "shot up." He was unwilling, however, to attribute this entirely to the effects of the radium. As to the permanent effect, my observations demonstrated that the pressure remained down for a considerable period after the patients discontinued treatment. In two cases of over 200 and one of 180 the pressure remained between 160 and 140 for three months after the emanation treatment was discontinued. These facts would seem to indicate the use of some form of radium for the reduction of high blood pressure. I am unable to account for this effect unless it be the action of the rays on the vessel walls, probably an inhibitory action on the vasomotor nerves. In only one case in which 100 micrograms was given was heart depression noted, consequently a central effect is, I believe, not probable with a reasonable dose. However, when possible I would recommend a course of emanation treatment to test the tolerance of the patient and this followed by an injection of not more than 50 micrograms.

The third section of my work has been concerned with the local application. For the past two months I have been using applicators containing the following amounts of radium element. (Please note that I

peak of radium element and do not mention the amount or the form of the salt used. This manner of quoting amount used has been adopted to secure uniformomenclature.) One square flexible varnish applicator, 36 square centimeters area, containing 5.6 milligrams of radium element; one rigid varnish applicator, nine square centimeters area, containing 24.2 milligrams of radium element ($\frac{1}{2}$ strength); one rigid varnish applicator, four square centimeters area, 21.4 milligrams of radium element (full strength), 10 milligrams of $\text{Ra Br}_2 \cdot 2\text{H}_2\text{O}$ per square centimeter area; one tube applicator containing 20 milligrams of radium element; three tube applicators containing each 50 milligrams of radium element; giving me a total of 21.2 milligrams of radium element equal to 413 milligrams of pure radium bromide or 290 milligrams of pure radium chloride. For ordinary skin lesions, such as soriasis, I have used 200 micrograms of radium element per ounce of ointment material.

A number of cases have been treated with one or a combination of the above-mentioned applicators, but I will give only a summary of my personal observations. All of my cases were apparently hopeless cancer. Under these circumstances I felt it my privilege and I now feel that it is my duty to make some contribution toward the technic employed rather than report results before sufficient time has elapsed.

With the aid of some of my medical friends it has been demonstrated that radium can be passed into the stomach through a gastroscope and held in position for at least thirty-five minutes. The same can be said when used with the aid of the laryngoscope, bronchoscope, etc. In the hands of an expert, then, almost every spot along these tracts may be rayed. It is obvious, however, that long and frequent exposures are impossible in such localities; therefore, enormous amounts of radium must be used if an effect is to be obtained.

By means of a rectal tube radium can

be applied to the rectum and sigmoid. By fixing tape to the free end, the tube can be held in place for a number of hours, especially when the introduction has been preceded by the placing of an opium suppository. It is not an easy matter to detect the point of ulceration in this locality. To overcome this one must secure measurements by the use of the proctoscope and, if this is not possible, the sensation of the patient (which can be elicited by passing a large tube) must be the guide. The application of radium to the vagina is a matter of secure packing and many special instruments have been provided for application to the uterus.

For universal application radium sealed in a tube is the most serviceable.

The requirement in the successful local application of radium consists in gaining exact knowledge as to the extent of tissue involved; in determining the amount of screening necessary; the length of exposure and the amount of radium to use. When we have solved these problems and can mathematically outline a definite technic for each individual case then and then only will we be able to say that radium in the hands of the general profession is a success or failure in the treatment of cancer. Until such a time the physicians whose technic has come from long experience and who commands the use of not less than 150 milligrams of radium element is the only authority qualified to give an opinion as to the therapeutic possibilities and results in internal cancer. As to skin lesions I believe that radium has already established its efficiency.

If my present experience is worth quoting then I say, without hesitation, that radium in small amounts for a large mass is harmful in that it stimulates rather than retards cell activity. The diseased tissue must be rayed throughout and rayed sufficiently to destroy cell activity. More than this, the rays should penetrate somewhat beyond the mass in order, if possible, to assist nature in forming a connective tissue

carrier, thus by healthy tissue wall off one source of general absorption. As a guide to the success or failure of this attempt I can suggest nothing at present other than the knowledge to be gained by daily differential counts. If the red cells increase, the leukocytes increase and then decrease, the patient is, perhaps, receiving sufficient radiation. For all easily accessible tumors covered by skin, I suggest incision for the purpose of burying the applicator in the mass, thus raying it from all directions besides avoiding danger of superficial burns. Mention should be made of the cross-fire method and its use is advisable wherever possible. All glandular involvement must so be sufficiently rayed. It has frequently occurred to me that hypodermic injections of an irritating substance containing small amounts of radium might be successfully employed to wall off slightly infected glands or nodules.

During this work I have had an opportunity to observe the effect of radium on the gross structure of a sarcoma.¹ This mass is located in the gluteal region.

It was operated upon and returned in two months. It was again operated upon and x-ray treatment used for one month.

It returned, in one month after close of second treatment, and grew very rapidly. When I first saw the case the mass was the size of half an orange and apparently well organized. Under radiation from 54 milligrams the mass greatly decreased in size, became deorganized, and is now, after radiation for an accumulation of 277 hours (which by the way is the largest accumulated dosage I have ever noted), coughing off and becoming free along the edges.

The exposed base gives the appearance of being healthy and the induration around the mass has been greatly lessened. The general condition of the patient is excellent and there has been considerable increase in weight.² This case has afforded excep-

tional opportunity to study the action of radium. The gross structure being entirely exposed, could be rayed without danger of seriously burning the skin. It is unfortunate that the many operations have caused this patient to object to specimens being secured from time to time for the minute study of the tissue.

In addition to the material used for the local application I have had access to large amounts of low-powered radium in the shape of radioactive earth, but as I have already taken up so much time with this subject I will not speak of the results obtained from its use. As for the use of the radium ointment for psoriasis the results in two extensive cases will certainly stimulate me to further investigation along this line.

If I seem to speak with undue enthusiasm regarding some feature of my experience with radium you will please consider that for the past five years I have devoted my entire time to the study of subacute and chronic conditions that in any way gave promise of being benefited by mechanical or physical agents. Success in many cases has been secured, but never have I been able to influence my so-called rheumatic patients to such an extent as I have with the use of radium in various forms. Even if the results obtained are not permanent certainly my results by other methods have not given even this satisfaction.

I take this opportunity publicly to thank the officers of the Radium Chemical Company of Pittsburgh not only for furnishing the radium for this work, but for their hearty co-operation in furnishing all the necessary appliances and skilled assistance.

My thanks are due also to many Pittsburgh physicians for clinical material, to Drs. Brill and Viol of the Radium Research Laboratory and Dr. Proescher of the Pathological Research Laboratory. I also consider it an honor to have been connected with the first free radium clinic in America.

¹On November 25 no sign of mass remains and wound almost entirely healed.

²Diagnosis not positive.

**Treatment of Malignant Disease of the Tonsil
with High Voltage X-Rays and Radium**

RICHMOND McKINNEY, M.D.
MEMPHIS, TENN.

*Reprinted from the Archives of Otolaryngology
July, 1933, Vol. 18, pp. 40-46*

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO, ILL.

3117
9A9390 MPOL
9A9391

Reprinted from the Archives of Otolaryngology
July, 1933, Vol. 18, pp. 40-46

TREATMENT OF MALIGNANT DISEASE OF THE TONSIL WITH HIGH VOLTAGE X-RAYS AND RADIUM

RICHMOND MCKINNEY, M.D.

MEMPHIS, TENN.

Doubtless one of the most hopeless sites of malignant growth at which to use treatment by radical surgical measures is the faucial tonsils, but in recent years there has been some hope offered in the treatment of the unfortunate patients through the medium of roentgen rays and radium, a therapy which seems to be showing a reasonable percentage of so-called cures. Even should this treatment not prove absolutely curative in most cases, the fact that one can by means of it give to the sufferers a prolonged and more comfortable life is in itself a constructive achievement in therapeutic progress.

Naturally one looks to the larger hospitals caring for patients with cancer for comparative statistics and for experimental work in treatment, as to these centers come patients from every direction, and such concentration gives an opportunity for study and experimental treatment that is not afforded the clinicians in smaller centers. Nevertheless, physicians who do not see many patients with cancer are just as vitally interested in the results of treatment and just as desirous of applying the best treatment, especially since most of their patients are financially unable to go to the hospitals for cancer in the larger cities.

In reviewing the case records of the Baptist Memorial Hospital, the largest hospital in my own city, where there are 425 beds, with an average admission rate of 11,500 per year, I found that during the past three years there have been only 6 patients with malignant disease of the tonsils admitted to the hospital, 2 of these having been under my care. On the other hand, Coutard¹ reported the results of treatment of only 46 patients with cancer in the tonsillar region with roentgen therapy at the Radium Institute of Paris during seven years, from 1920 to 1926, inclusive. Considering the large number of patients with cancer who apply at this institute for treatment, the number of patients with malignant growths of the tonsil who have been treated at the Baptist Memorial Hospital during a three year period is not comparatively small. There have been a number of patients with oral cancer admitted

Read at the Fourth Pan-American Medical Congress, Dallas, Texas, March 21, 1933.

1. Coutard, H.: *Radiophys. et radiothérapie* 2:541, 1932.

to the hospital, but I shall consider only those in whom the condition was limited to the tonsillar region. Duffy² reported and reviewed 122 histologically proved cases of cancer of the tonsil treated at the Memorial Hospital from 1921 to 1928, inclusive. Berven³ reported 42 cases of carcinoma of the tonsil treated between 1919 and 1927.

Coutard treated his patients with roentgen therapy alone. He claimed that in the series of 46 cancers of the tonsillar region already mentioned, 12, or 26 per cent, were cured. No local recurrence developed in any of the patients, and the proportion of metastases occurring more than two years after treatment was 1 in 12, or 8 per cent.

Coutard said that since 1926 the results of treatment of cancer of the tonsillar region have improved; that the primary cancer and glandular invasions have been cured in 46 per cent of the cases—which sounds extraordinary to me.

Duffy classified his cases into early and advanced, according to the extent to which the lesion had spread. Of the 122 cases, 33 were early and 88 advanced. Only 51, or 41.8 per cent, of the patients were without cervical metastases when admitted. His method of treatment is as follows: A combination of external and interstitial irradiation is used. High voltage roentgen therapy is applied to each side of the neck, the beam including both the primary lesion and the areas of lymphatic drainage. Immediately after this, the radium pack is directed over the primary lesion and the adjacent cervical region. Full erythema doses are used. This amount of radiation delivers from 150 to 180 per cent of a skin erythema dose to the tonsillar region. Radon is then implanted in the neoplasm.

The amount of radon needed is judged from the histologic grade of the tumor, its size and shape and the clinical response to external irradiation. In some cases in which there are operable metastases, dissection of the neck is performed when the cutaneous reaction is about healed. If the primary growth is of a highly radiosensitive type, radical surgical treatment of the nodes is not undertaken, dependence being placed on the surgical exposure of the node and the implantation of radon in full dosage in gold tubes. In the more advanced cases, the interstitial irradiation is buried through the skin without incision. The latter method is used in the treatment of advanced inoperable growths, whether the type cell of the neoplasm is radiosensitive or radioresistant.

In order to evaluate the efficacy of external irradiation, Duffy considered the patients in two groups. The first group included those treated between 1921 and 1924, inclusive. About 1925 the dosage for external irradiation was increased, and later 4 Gm. of radium element

2. Duffy, J. J.: Surg., Gynec. & Obst. **54**:539 (March) 1932.

3. Berven, E. G. E.: Strahlentherapie **42**:113, 1931.

pack was added to the hospital equipment. In the earlier group, 50 per cent of the patients remained free from regional metastases, and 66 per cent of those living two years or longer had no evidence of cervical involvement. For the later group, the corresponding percentages were 72 and 77. After the beginning of 1925, gold tubes replaced glass seeds. They were found much more efficacious in the destruction of the primary growth; the percentage of local recurrences decreased from 30 to 24 in the later period. Necrosis, with subsequent slough and hemorrhage, caused much trouble when the glass seeds were used. There has not yet been sufficient time to judge the five-year results in the group treated since 1925. The material before 1925 consisted of 49 cases; 10, or 20.4 per cent, of the patients survived the five-year period. One patient died without cancer just at the close of this period. If this case were added, the percentage would be 22.4.

Of the 13 patients who had no cervical involvement throughout, 5, or 38.4 per cent, are well. In 13 metastases developed after admission; none of these is well. Fifteen had operable nodes on admission, and 4, or 26.6 per cent, are well. One of the 8 who had inoperable nodes on admission is well.

Duffy concluded that carcinoma of the tonsil should be treated by irradiation therapy, or by irradiation and surgical treatment for certain metastases, but not by surgical treatment alone.

Berven, reporting on his series of 42 carcinomas of the tonsils, said that from 1919 to 1924 he treated the carcinomas with the x-rays from the outside, and with radium screens placed on the tumor on the inside. In his series of 23 patients thus treated there was no permanent cure, the period of freedom from symptoms being less than three years. Since 1924 he has been treating with radium as follows:

The radium is applied on three or four fields: (1) over the neck on the side of the tumor, (2) over the opposite side, (3) over the posterior part of the neck and (4) over the cheek. Six tubes, 11 by 2.5 mm., are applied for one hour each; filtration consists of 0.35 mm. of aluminum plus 0.3 mm. of platinum, the total filtration, with the applicator, being equivalent to 5 mm. of lead. The tubes are placed over a circular area about 5 cm. in diameter. The surrounding tissue is protected by 6 cm. of lead. The applicator is 6 cm. from the skin. About 30 per cent of the surface intensity reaches the tonsil from the area on the same side.

Of 14 patients treated from 1923 to 1927 with the new technic, 4 or 28.6 per cent, did not improve; 4 improved, 1 living nearly four years; 2 were free from symptoms for thirteen and twenty-seven months, respectively, and 4 were free from symptoms for three, four, four and one-half and five and three-fourths years, respectively.

In discussing the differential diagnosis between syphilis and malignant tumor, Berven stresses that antisyphilitic treatment can reduce the necrosis and the size of a malignant tumor, particularly if syphilis is also present. This clinical fact is borne out in the history of a case I shall presently report.

The statistics just quoted, taken mostly from abstracts in the 1932 "Year-Book of Radiology," give a comprehensive and an analytic consideration of the occurrence and treatment of malignant disease of the tonsillar region. They are of value to the surgeon who sees an occasional case, and who naturally seeks to use for his patient the most approved method of treatment, and the one that gives the greatest promise of prolonged life or of a cure in the accepted sense.

I was interested in a talk made by Dr. Henry Schmitz ⁴ of Chicago before a meeting of the Southern Interurban Obstetrical and Gynecological Association in Memphis, on Feb. 13, 1933, in which he argued for the use of high voltage roentgen treatment for patients with cancer rather than the application of radium, largely for reasons of economy and availability. He stated that there are approximately 90,000 cases of cancer annually in the United States, and that to treat all the patients with radium would be impossible. He said that roentgen treatment would accomplish just as much in these cases, and would cost only about one-ninth as much as radium. By the establishment of centers for high voltage roentgen therapy throughout the nation, the 90,000 patients could receive treatment at a total cost of about \$11,000,000, whereas to treat the same number of patients with radium would cost \$97,500,000, if the radium could be found.

Coutard is using high voltage roentgen treatment exclusively, and from a colleague who has recently returned from Paris, where he visited Coutard at the Radium Institute, I learned that he is using an intensive form of high voltage roentgen therapy for cancer of the tonsil as well as of other portions of the body, the technic and results of which he is not yet ready to describe. So far as I can learn, the method consists in treating the patients twice daily, the rays being filtered through a screen that would be the equivalent of 2 mm. of copper. The same areas of exposure are treated as with the old method, but with the filter that he uses he seems to get rid of the alpha and beta, or burning, rays entirely, which are filtered out, and gets only the gamma, or curative, rays. He is thus able to use frequent and intensive treatments. One patient with cancer of the tongue involving the tonsil was shown to my colleague; he had received 10,000 roentgens over a period of sixty-six days, twice daily, corresponding to 18 or 20 erythema doses. This patient's

4. Quoted in Memphis Commercial Appeal, Feb. 14, 1933.

skin showed no hardening, but a decided bronzing. From 5 to 8 patients who were taking this intensive treatment without burns were seen daily. Coutard stated that he does not hesitate to give the treatment indefinitely, so long as the patient does not show a systemic reaction. Coutard expressed himself as believing that in a few years high voltage roentgen treatment for all kinds of cancers will entirely supplant surgical treatment.

When palpable glands of the neck are found in malignant conditions of the tonsil, it is generally regarded as good practice to use block dissection. This should be complete, involving ligation of the external carotid and resection of the sternocleidomastoid muscle and the jugular vein. There is doubt, from the experience of some investigators, as to whether this really is of much worth in preventing glandular dissemination, the argument being that if the glands have become involved to such an extent, the chances are that the removal of these palpable glands may be useless, since glands lower down may be involved. However, it is the opinion of the majority of surgeons who have had extensive experience with cancer of the oral cavity that cervical block dissection, after the application of radon seeds and high voltage roentgen therapy, is attended by the most favorable results. Dr. Shields Abernathy of Memphis, a general surgeon with whom I have been associated in the application of radium in several cases and who has had considerable experience in the treatment of cancer of the oral cavity, has found that the cases in which he has used block dissection following the customary irradiation have given the most lasting results. I have seen some of his cases in which more than five years after such treatment there was no evidence of recurrence either at the original site or by metastasis. It is sometimes rather difficult, if not impossible, to persuade a patient who has been cured by irradiation so far as he is concerned to consent to an operation. If an operation is necessary, there should be a definite understanding with the patient before the application of radiation that he is to have the block dissection.

My observation and experience in the treatment of malignant disease of the tonsils have been with the combined use of radon implants and high voltage roentgen therapy. I shall now submit a report of 2 cases in which the technic and immediate results obtained by this method are clearly portrayed.

REPORT OF CASES

CASE 1.—A woman, aged 42, was first seen on Aug. 18, 1931, with the history of having a swelling in the right faucial tonsil for some weeks. There was pain shooting through the ear on this side, and there had been some loss of weight. There were no palpable glands in the neck, but she was anemic.

Examination showed a large new growth of the right faucial tonsil, extending from the tip of the lower lobe to the velum palati and over the right faucial pillar.

With punch forceps two fairly large portions of tissue were removed from the growth for histologic examination. The report from the laboratory of the Baptist Memorial Hospital was that the growth was a lymphosarcoma, with many mitotic figures in the tissue.

On August 27, after I had anesthetized the involved area with procaine hydrochloride, Dr. Abernathy placed ten radon gold implants in the surrounding tissues and throughout the growth. The next day the patient left the hospital. On September 24, she returned for high voltage roentgen treatment. On four successive days 342 roentgens was applied through a 0.5 mm. copper filter to the following areas: first day, the posterior part of the neck; second day, the right lateral part of the neck; third day, the left lateral part of the neck, and the fourth day, the right lateral part of the neck.

The patient was sent home; when she returned for further inspection on Jan. 22, 1932, it was found that the lesion had entirely disappeared, and that she was feeling fine. I have seen her again in recent months, and there is not the least evidence of recurrence at the original site or anywhere else in the body.

Lymphosarcomas are peculiarly susceptible to treatment by radiation, but they frequently are rapidly fatal. Case 1 is a splendid example of the benefit to be derived from irradiation of this type of growth. I shall watch with much interest the subsequent progress.

CASE 2.—A man, aged 68, was brought to me during the latter part of October, 1932, with the statement that for more than two months he had a growth on the right faucial tonsil, with enlargement of the glands of the neck on that side, for which he had been receiving treatments by local application, doubtless of nitrate of silver. He had very little pain, and had lost practically no weight.

A large, ragged growth involved the entire area of the right faucial tonsil, with marked extension into the soft palate and the pillars of that side. The cervical glands were greatly enlarged and very hard.

With punch forceps two large portions of tissue were removed from the growth, and blood was taken for a Wassermann test. The laboratory reported that the growth was a squamous cell epithelioma of the tonsil, and that a patient had a 4 plus Wassermann reaction.

Preliminary high voltage roentgen therapy was begun immediately, the dates and dosage being as follows: On October 10, 200 roentgens to the posterior part of the neck through a 1 mm. copper filter; on October 27, 342 roentgens to the right lateral side of the neck through a 0.5 mm. copper filter, and on October 28, 342 roentgens to the left lateral side of the neck through a 0.5 copper filter.

On October 28, with the patient under local anesthesia with procaine hydrochloride, Dr. Abernathy placed twelve radon gold implants in the surrounding tissue and the center of the growth. The patient returned home the same day, and I started him on intensive treatment with iodide of potassium.

Within a month the growth had entirely disappeared, the involved area was perfectly smooth, and there was just one small palpable gland, about the size of a buckshot. The patient refused block dissection.

It is too early to venture an opinion as to results in case 2, but the patient will be kept under observation and will receive further high voltage roentgen treatments from time to time.

COMMENT

I am of the opinion that malignant disease of the tonsil is treated most satisfactorily by blocking with high voltage roentgen treatment, implantation of radon gold seeds, dissection of the neck in a thorough manner and further high voltage roentgen treatment in the order given. A radical attack on the glands, either by interstitial irradiation or by surgical removal, should never be made until the primary lesion is treated, for that lesion is the distributing point not only for the cancer cells, but also for possible infectious conditions.

It would be very dangerous if patients were subjected to high voltage roentgen treatment alone at the hands of indiscriminate roentgenologists, for this treatment is capable of good results only when applied in carefully regulated doses and by a skilled roentgenologist. However, if Coutard's expectations are realized, surgical intervention in these cases may eventually be supplanted by intensive high voltage roentgen treatment.

My experience has been that of a rhinolaryngologist to whom these patients have come on account of conditions of the throat. I have felt happy to be so situated that I could have the aid of a competent general surgeon in this work and of the x-ray laboratory of the Baptist Memorial Hospital, which is well equipped for obtaining good results in the application of roentgen therapy.

899 Madison Avenue.

RADIUM IN DERMATOLOGY

O. H. FOERSTER, M.D.
MILWAUKEE

Reprinted from the Archives of Dermatology and Syphilology
January, 1924, Vol. 9, pp. 38-50

COPYRIGHT, 1924
AMERICAN MEDICAL ASSOCIATION
FIVE HUNDRED AND THIRTY-FIVE NORTH DEARBORN STREET
CHICAGO

RADIUM IN DERMATOLOGY

O. H. FOERSTER, M.D.
MILWAUKEE

RADIUM IN DERMATOLOGY *

O. H. FOERSTER, M.D.

MILWAUKEE

The rational and successful application of radium therapy requires a knowledge of the fundamental physical properties of radium and of the biochemical tissue reactions to radium energy.

In the continuous process of spontaneous disintegration of radium, there are produced alpha and beta electromagnetic particles or rays and gamma rays, the latter being nonmaterial electromagnetic pulsations of the ether. The alpha particle is the nucleus of a helium atom with two positive charges of electricity, and because it is readily absorbed by the glass container or the varnished surface of an applicator, is of negligible value in radiotherapy. Beta rays or particles are negative electrons of varying high velocity with corresponding differences in their power of penetration. Those of low speed are absorbed by from 1 to 5 mm. of aluminum, and 2 mm. of lead will absorb all beta rays (Failla). Gamma rays are of different wave lengths and are extremely penetrating, requiring 1.4 cm. of lead or 6.24 cm. of aluminum for 50 per cent. absorption. In the decay of radium the powerfully radioactive gas, radium emanation, is produced, which by its further decay forms radium A, B and C. These three bodies, which emit alpha, beta and gamma rays, constitute the radio-active deposit of rapid change which is formed on the walls of the tube or other container in which the emanation is sealed.

When beta or gamma rays impinge on matter secondary radiations are produced which vary in their intensity with the density of the obstructing material and the intensity of the primary ray. Beta rays give rise to secondary gamma rays, which in turn give rise to tertiary beta rays, and the primary gamma rays produce secondary beta rays of marked penetrating power. The production of these secondary corpuscular rays in the tissues is thought to be the basis for the biologic or therapeutic effect of radio-active agents.

There is a wide variation in the penetrating power of the beta and gamma rays. Approximately one-half of the beta rays from an unscreened surface applicator are absorbed by a thickness of 0.05 mm. platinum, 0.1 mm. lead, 0.11 mm. silver, 0.13 mm. brass, or 0.4 mm. aluminum, and practically all of the beta rays are absorbed by thick-

* Read at the Forty-Sixth Annual Meeting of the American Dermatological Association, Ann Arbor, Mich., June 7-9, 1923.

nesses of 0.4 mm. platinum, 0.8 mm. lead, 0.9 mm. silver, 1.1 mm. brass and 3.2 mm. aluminum. Colwell and Russ have also determined that the intensity of the hard beta rays is reduced to about 6 per cent. of the initial value after passing through 1 cm. of epithelial tissue. One half of the gamma rays are absorbed by 6.24 cm. aluminum, 1.14 cm. lead and 1.4 cm. silver. It may be stated as a general rule that the absorbing power of a substance for a given type of beta or gamma ray increases in proportion to its density. Furthermore, the absorption of beta rays of high velocity ("hard" beta rays) and of gamma rays of any given wave length follows closely an exponential law to the effect "that an equal thickness of the same material absorbs the same fractional amount of the incident radiation. Thus, if initial intensity is reduced to half value by 1 mm. of aluminum, 2 mm. of aluminum will reduce the initial value to one-fourth" (MacKee).

The intensity of radiation is further reduced by distance in accordance with the inverse square law, that is, doubling the distance reduces the intensity to one-fourth.

These facts provide the physical basis for filtration by means of which a selection of rays suitable for superficial or depth action is possible. Filtration is of prime importance in radium therapy, for it is evident that the factor of importance in treatment is not the quantity of radium available as a source of energy, but rather the quantity and also quality of the radiation that actually penetrates the diseased tissue. Only absorbed energy can exert biologic action.

In dermatology radiation for both superficial and deep effects is required. Owing to the high percentage of low speed or "soft" beta rays in the radiations from unfiltered surface applicators, these are employed for surface effects only, in disorders with slight thickening of the skin. In order to influence pathologic conditions extending to a depth of 1 cm. or more filtration is required so as to eliminate the superficially absorbed "soft" beta rays, and to utilize the penetrating beta rays of high velocity. Without such filtration the superficial strata will be overdosed with "soft" beta rays before the desired quantity of "hard" beta rays can be absorbed by the deeper parts. A quality of ray suitable for dermatologic work is the "surpenetrant" ray composed of hard beta and gamma rays, and obtained by filtration with 0.1 mm. of silver or lead. In lesions or growths of greater thickness than 1 cm., or in those situated more than 1 cm. below the surface, the penetrating qualities of the gamma rays are utilized. By suitable heavy filtration all the beta rays and, if desirable, the gamma rays of long wave length, can be eliminated and a homogeneous type of gamma radiation obtained. Such filtration secures a fairly uniform intensity of radiation in the tissues for a distance of several centimeters.

The employment of filters introduces the additional factors of secondary radiation generated in the filter material and of loss of intensity through increased distance. The secondary rays formed in the various metallic filters are very superficial in their action and quite irritant, but are completely absorbed by 0.2 mm. of aluminum, and one or two layers of rubber dam will eliminate the soft rays produced in the aluminum. The use of thick filters increases the distance and results in a loss of intensity which varies inversely as the square of the distance. In addition, filtration influences the exposure time to a marked degree, in part by increase in distance, though chiefly through absorption by the filter material. The use of dense metals such as filters, owing to decrease in thickness, allows close approximation with consequent reduction in the exposure time.

In the absence of radiometric methods for standardizing radium dosage, it is necessary personally to standardize applicators, needles and tubes as used in dermatology, according to time and skin effects. With known strength, the time required to produce an erythema under varying conditions of filtration and distance is thus empirically determined for every applicator. Based on such experience, it is possible to secure any desired degree of reaction varying from a mild erythema to ulceration. Consideration must be given, however, to differences in individual susceptibility due to sex, age, color and texture of skin, and more particularly to location. True idiosyncrasy is rarely observed.

BIOPHYSICS AND BIOCHEMISTRY

The stoppage or absorption of the primary beta and gamma rays in their passage through tissue results in the production of secondary or corpuscular rays, to whose ionizing action are attributed the biologic effects produced by radium. The beta rays, being more readily absorbed, it is assumed that their passage is associated with a greater production of corpuscular rays and therefore of a greater amount of ionization than that which attends the passage of gamma rays. The ability to stop or break up the radiations varies directly with the atomic weights of the interposed atoms and molecules. The mineral content of the tissues is therefore of importance in the production of secondary rays and in the amount of ionization produced. The phenomena attendant on ionization are thought to vary with the stability or instability of the chemical activity of the tissue cells, but whether ionization produces its results through direct chemical reactions, nuclear disintegration or enzyme action, is an unsettled question.

The variation in the chemical composition of cells as well as variation in growth activity determines the degree of change induced by

radiation; the same quantity or quality of rays absorbed therefore produces quite different biologic effects at the same time in different cells or at different times in the same cell. This characteristic of radiant energy has been termed selective action. In contrast to this there is a differential action induced by different qualities or quantities of radiation acting on similar tissue.

Variation in quality of rays is an especially important factor and leads to the choice of variable filtration in different diseases or in different instances of a similar disease. The determination of filtration and dosage is based on the requirements of the individual case, and is not entirely subject to standardization. With the wide range in qualitative variation, especially among the beta rays, mathematical standardization of dosage, so satisfactorily established in roentgen-ray therapy, cannot be carried out without losing some of those particular advantages inherent in the wider range of radium radiation over the comparatively homogeneous roentgen rays.

The range of biologic action dependent on quantity of radiation extends from stimulation to inhibition and then destruction, and it is thought that increased metabolic or chemical activity through stimulation can by overstimulation produce destruction through exhaustion. Cells most susceptible to such destructive stimulation are embryonic cells, or rapidly dividing cells, such as malignant cells, and cells of inherent metabolic instability such as lymphoid cells, gland cells and endothelial cells. In the human skin the cells of the germinal layer, hair papilla, and of the glands, the endothelial cells of the capillaries and the fixed connective tissue cells are highly radiosensitive, whereas the non-nucleated elements of the skin—the corneous layer, hair, the elastic and collagenous connective tissue—are much less, or only slightly, susceptible. The cell changes in the susceptible tissues consist essentially of nuclear swelling, with vacuolization and later hyaline degeneration, and in addition there are early and persistent inflammatory changes, seen chiefly in the papillary layer and consisting of perivascular infiltration and edema, with deposition of pigment. It may be noted here that a direct bactericidal action of radium rays on bacteria in tissues, without serious damage to the tissues, cannot be obtained.

In therapy it must be determined whether an inhibitory or destructive action is desired, and in case of the latter whether destruction and removal of diseased tissue shall be by gradual resolution or cellular disorganization and cytolysis with associated connective tissue proliferation, or by an intensive reaction resembling cauterization and destroying pathologic and normal tissue alike within a given radius. The latter mode of action is best carried out by injection of radium needles or

emanation tubes, but can be obtained superficially with the unfiltered soft beta rays through intensive ionization.

In dermatology a purely stimulating action attributed to radium rays finds only limited application, whereas, according to MacKee, in most cutaneous disorders that are amenable to irradiation the therapeutic effects are explainable, with reservations, by the assumption of an inhibitory or retarding action on cell division.

A valuable contribution to this phase of the subject has been made recently by Highman and Rulison.¹ They offer an explanation based on the histopathology of various dermatoses for what may be expected of roentgen rays in therapy, much of which applies to radium as well.

INDICATIONS

The experience of many years has established radiotherapy as an effective method for the treatment of basal cell epithelioma. The derivation and character of the cells composing this new growth are such as to indicate that it is susceptible to irradiation by both radium and roentgen rays. Preference is given to radium in the treatment of these growths when they are located on the eyelids or at the canthi, on or behind the ear, in the nasolabial fold, or when the nasal or buccal mucosa is involved. It is my belief that in these locations at least, radium is more effectual than are roentgen rays, and secures better end results with fewer recurrences.

The technic of treatment as given by different writers indicates a preference for filtered rays predominantly of the harder beta type, with less of the beta and more of the gamma rays when the growth is thick, nodular or deep-seated. Direct contact rather than distance radiation is used, except in the deep-seated growths, and in such it is probably best to follow Morrow and Taussig's² advice to insert bare emanation tubes or steel needles. My results with steel needles in dense, nodular growths located in the eyelid are undoubtedly better than with surface applicators. The total exposure time is usually divided between two or three days, followed by a second less intense series after an interval of from four to six or eight weeks if evidence of disease remains, or a single, more intensive dose may be given and repeated after an interval averaging four weeks.

The prognosis is modified unfavorably when the base of the epithelioma is firmly attached to the underlying structures, with involvement of the periosteum, bone or cartilage. In such cases intensive

1. Highman, W. J., and Rulison, R. H.: *Tr. Sect. Dermat. A. M. A.*, 1922, p. 195.

2. Morrow, H., and Taussig, L.: *Am. J. Roentgenol.* **10**:212 (March) 1923.

destructive radiation is required, and is often followed by the separation of a sequestrum to which the remains of the growth may be attached. Involvement of the cartilage of the ear, if not too extensive, does not contraindicate the use of radium; in this location ulcerated basal-cell growths, 4 sq. cm. in size, have healed with remarkably little deformity. In most instances, however, in which there is involvement of bone or cartilage, it will be found advisable to employ electrocoagulation, as advocated by Pfahler and Clarke, followed by radium. While, as Morrow remarks, the question of preliminary curettage is still an open one, this method as well as preliminary electrocoagulation has advantages in the case of nodular, dense or deep-seated lesions, and appears to decrease the percentage of recurrences. Electrocoagulation is preferred to curettage by many, including myself.

Epitheliomas that have failed to respond to long continued treatment with roentgen rays, or to treatment with caustics, carbon dioxid snow, electrolysis and other similar measures, or that recur after such treatment, frequently prove refractory to radium. A special problem is then presented owing to the diminished vitality of the tissues bordering on the growth and beneath it, which requires that radium, if employed at all, be used with caution and careful judgment to avoid undue reaction, which may follow even on much reduced dosage, with subsequent ulceration of trophic type.

It appears to be the rule of most writers with large experience to limit the irradiation treatment of squamous or prickle cell epitheliomas to those which are recognized in an early stage and are small and superficial. Well developed cases of this type of epithelioma, even when not accompanied by palpable lymph glands, should for the present at least, be treated by other procedures, preferably surgery. When irradiation is indicated it should be intensive, employing the hard beta and the gamma rays, and cross-firing if possible, without regard for the cosmetic result. Some writers, such as Morrow and Taussig, advise the use of unscreened tubes of emanation or of steel needles containing radium element in addition to surface radiation, and do not hesitate to attack the more advanced types of prickle cell epithelioma by this combined treatment. Others, notably Pfahler and Clarke, advocate a combination of desiccation, radium and roentgen rays as useful even for the treatment of far advanced cases. It is the general opinion that intensive irradiation of the regional lymphatics, whether nodes are palpable or not, with heavily filtered roentgen rays, is an essential part of the treatment. If the growth and the glands are removed surgically, treatment with roentgen rays should precede, and more especially follow, the operation, as this improves the chances of eradicating the disease.

In prickle cell carcinomas of the nose, Sutton³ has obtained the best results by the radical use of the knife cautery followed by radium or roentgen rays. In prickle cell growths of the ear, when more than 1 cm. in diameter, Morrow and Taussig advise that they be "thoroughly curetted, cauterized, preferably with pure chromic acid or the actual cautery, and then rayed cautiously; the smaller lesions may be treated with radium alone." It may be noted here that cures of roentgen-ray epitheliomas with radium have been recorded by Abbe and MacKee.

The literature on radiotherapy in sarcoma cutis recounts chiefly the effects of roentgen rays, for radium has been used in only relatively few instances. With intensive radiation as used for epithelioma good results have been obtained with radium in fibrosarcoma and in the rare giant-cell type. Melanotic sarcoma most often is radioresistant, and although the primary tumor may be inhibited in its growth or at times destroyed, distant metastases are almost certain to develop. The lesions of idiopathic multiple hemorrhagic sarcoma are highly radio-sensitive. Beta rays of a quality obtained by filtration with 0.1 mm. of silver, and in a dose sufficient to effect an erythema, cause individual lesions to disappear, but new lesions usually develop, and almost continuous treatment is required to control the disease.

Many of the keratoses may be treated successfully with radium. The scaly type of senile keratosis, which is often refractory to roentgen rays, yields readily to soft beta rays in a dose large enough to produce a mild erythema; the nevoid and verrucous types, however, require a hard beta or gamma quality of ray for their destruction, but frequently prove resistant even to intensive dosage. Preliminary curetting is preferred by MacKee, and others employ fulguration. Keratoses on the mucous membrane of the lips respond well to radium, and filtration with 0.1 mm. of silver secures a suitable quality of ray for most cases. I share MacKee's belief that the dose should always be of sufficient intensity to produce a sharp inflammatory reaction. In the treatment of roentgen-ray keratoses and the keratoses occurring in xeroderma pigmentosum, both of which as a rule respond well to radium, it is advisable to select a beta quality of ray that will expend its energy chiefly in the epidermis and upper corium, with but minimal effect on the profoundly altered deeper tissues.

Concerning leukoplakia, opinion is divided as to the advisability of its treatment with radium, and if so treated as to the type and intensity of radiation to be used. It will be generally conceded that in this potentially malignant condition any measures of treatment which are not thoroughly and powerfully destructive are meddlesome and dangerous. Although good results have been obtained with radium, notably

3. Sutton, R. L.: *Tr. Sect. Dermat. A. M. A.* 1921, p. 161.

by Abbe, Degrais and Knox, it is the general view that the effects of treatment are uncertain and that recurrence is frequent, except in small and thin lesions. It would seem that prolonged treatment with heavily filtered radium, as advocated by Knox and others, is destined to produce undesirable deep effects that cannot be disregarded, especially when vascular changes exist such as occur in late syphilis.

If treatment with radium is undertaken, irradiation of an intensive type, resembling cauterization and limited in its effects to the epidermis and upper corium, would seem best to meet the indications. Simpson employs a dose described as "caustic," and at times gives "deeper and less caustic radiations" using the emanation. MacKee prefers for the present to remain noncommittal on this question, although he advises that beta rays (filtration with 0.1 mm. aluminum, and in verrucose forms 1.0 mm. aluminum) may be used in destructive dose, and if not promptly curative that irradiation should give way to some other method, such as the electric cautery.

In the treatment of keloids and hypertrophic scars irradiation is the method of election. The response to treatment varies with the size, thickness, consistency, rate of growth and duration of the lesion, experience having shown that recent, small, soft, rapidly growing keloids, especially those occurring in young subjects, are most susceptible to irradiation. The clinical response to roentgen rays or radium is not essentially different, though Simpson and others express a definite preference for radium. Pfahler ⁴ claims superior results from a method in which excision is preceded and followed by irradiation with either roentgen rays or radium. In extensive lesions, roentgen rays find a special indication, and because of convenience and perhaps greater effectiveness, radium appears to be especially applicable in localized hypertrophies in scar tissue, keloidal bands, and lesions in special locations or where cross-firing is possible. The aim of treatment is to produce gradual absorption of the growth with least injury to the overlying epithelium. A primary requirement is the elimination of all the soft beta rays. While hard beta rays are often used, especially for lesions less than 1 cm. thick, the general preference is for gamma radiation secured by filtration with from 0.5 to 1 mm. of silver or 1 mm. of brass, in a dose producing a mild erythema, which may be repeated in about six weeks. In children the dose should be reduced to one half or one fourth of the adult dose. It is desirable to screen out the secondary rays formed in the heavier filters by the use of 0.1 or 0.2 mm. of aluminum and one or two layers of rubber dam. Old, fibrosclerotic keloids will sometimes yield to hard beta radiation in

4. Pfahler, G. E.: Tr. Sect. Dermat. A. M. A., 1920, p. 230.

destructive dosage, leaving a relatively good scar, but such treatment is not recommended for general adoption.

The exposures for keloid are made with flat applicators or tubes retained in close contact with the lesion, and placed so as to include all of the peripheral prolongations without exposure of the normal skin. Repeated applications are usually required, with variation in dosage according to the response to the preceding treatment. It is necessary that good judgment be used in determining intensity and spacing of dosage to minimize atrophy, pigmentation and especially telangiectasia, which is prone to occur in keloidal tissue.

In selected cases of vascular nevi radium is a most satisfactory therapeutic agent. It is in this field that the most exacting demands are made on the technical skill and good judgment of the worker with radium, because the prime object of treatment is to obtain a satisfactory cosmetic effect. Treatment of these conditions should not be undertaken except by those skilled in the use of radium, if disappointing or even disastrous results are to be avoided.

For present purposes vascular nevi or angiomas are considered under three clinical types (MacKee): nevus flammeus (portwine mark), nevus vasculosus (strawberry mark), and angioma cavernosum (cavernous angioma). The histopathology of these types offers an explanation for the variations observed in their response to irradiation, and in this connection the following is quoted from MacKee:

The elevated types of nevus vasculosus yield to radium in the most striking manner. Even the cavernous nevus will disappear under safe therapeutic dosage. It seems paradoxical but the superficial port-wine mark is exceedingly recalcitrant. The types that respond well begin after birth and continue to increase in size for weeks and months. There is a numerical increase in the blood vessels which are dilated, abnormally cellular and which continue to develop by budding processes. In other words, a new growth in which the cells are more or less embryonic in type. When irradiated it is probable that mitosis is arrested, new vessels cease to form and finally the poorly differentiated cells composing the vessels fail to be replaced and are absorbed. The troublesome port-wine mark is fully developed at birth, the cells are mature, well differentiated and not very active. It can, perhaps, be likened to telangiectasia. To cause an obliterating endarteritis in telangiectasis, spider nevus and port-wine mark requires an amount of treatment that may seriously injure normal tissue.

Most writers agree that the treatment of nevus flammeus with radium is inadvisable and that satisfactory results are the exception. Abbe⁵ and Simpson emphasize that treatment requires caution and skilful technic. Simpson employs a 1/20 strength screened "toile"

5. Abbe, R.: Urol. & Cutan. Rev. **25**:65 (Feb.) 1921.

applicator and insists that an inflammatory reaction must be avoided. Abbe uses 0.1 mm. of lead as a filter and to avoid a spotty effect slowly moves the applicator over the area during the entire duration of the treatment, which is not repeated for three months.

Nevus vasculosus or strawberry mark is responsive to irradiation, and it is generally conceded that the best effects are obtained with beta rays. Some prefer to use tubes and distance radiation, but the general preference is for flat applicators retained in close contact with the lesion by firm pressure. According to the thickness of the nevus, filtration with 0.1 to 0.4 mm. of aluminum is selected, with one or two layers of dental rubber dam to screen out the secondary rays. Thin lesions may be successfully treated with the unfiltered beta rays. The time of exposure should be slightly less than that required to produce an erythema, and is to be considerably reduced if the nevus has been previously treated with carbon dioxid snow or other measures. Subsequent treatments may be given at intervals of three or four weeks, the dose, usually less intense, being regulated according to the effects of the preceding treatments. In the treatment of all angiomas the skin adjoining the nevus should always be protected from the action of the rays.

Excellent results are obtained in angioma cavernosum with radium, especially in the smaller and more superficial lesions occurring in children. Massive, deep-seated angiomas in adults are apt to prove refractory. MacKee states that "beta rays are by far more efficacious than are roentgen rays or gamma rays when the lesion has a depth of not more than two or three centimeters," and that "for deeper lesions there seems to be little if any difference between the effect obtained with roentgen rays or gamma rays," although he prefers and advises the use of radium. Newcomet⁶ advocates the use of tubes and radiation from a distance in cavernous angioma, a method that is especially adapted to the treatment of deep-seated, subcutaneous and submucous tumor-like angiomas. In such cases Simpson prefers plaques of emanation or radium to tubes, and also employs distance radiation. In cavernous angiomas the element of distance or depth may sometimes be diminished by causing more or less collapse of the lesion by firm compression, and in favorable locations or when the nevus is raised advantage may be taken of the opportunity to cross fire.

Cavernous angiomas exhibit such variation in clinical features and in their individual response to irradiation that the technic of treatment cannot be expressed in other than general terms. In most cases flat applicators are used, and are retained in firm contact with the nevus. The filtration may vary from 0.1 to 1 mm. of aluminum or its equiva-

6. Newcomet, W. E.: Am. J. Roentgenol. **7**:337 (July) 1920.

lent in other metals, according to the depth of action desired. The dose should not exceed that required to produce a moderate erythema, "short of blister," according to Abbe,⁵ though Pfahler⁷ and others obtain excellent results with the use of smaller doses. It seems desirable not to proceed too confidently on the basis of previous experience, but to remain within safe limits of dosage for the initial treatment, and use the effects obtained as a guide for subsequent treatments. The intervals between treatments should be from four to eight weeks, and the entire period of treatment may extend over one or more years. The regressive changes in the tissues take place slowly and treatment must be conducted with judgment and patience if undesirable sequelae are to be avoided. Pfahler's advice, like that of all experienced workers with radium, is to proceed slowly and carefully.

Lymphangioma circumscriptum of the skin and mucous membranes responds to hard beta radiation with a technic similar to that employed for vascular nevi of the strawberry mark type. I have observed a tendency to recurrence after apparent cure of cutaneous lesions, which is not exhibited by the vascular nevi, and which confirms MacKee's observation that the response to treatment is less rapid than in vascular nevi. Simpson says that "in lymphangiomata affecting the mucous membranes and particularly the tongue, radium is of unique value and can hardly be replaced by any other agent," a statement which is supported by my rather limited experience.

After many years of observation the value of radium in the treatment of lupus erythematosus still remains a debatable subject among dermatologists. It would appear on histopathologic grounds, as suggested by Highman and Rulison,¹ that indications are lacking for the use of radio-active agents in a disease that shows vascular dilatation and destruction of the elastic tissue and ends in atrophy, all of which are tissue changes that can also be produced by radium. On the other hand and on similar grounds, it may be argued that by the use of radium results may be obtained analogous to those that are probably produced during the spontaneous involution of lupus erythematosus. It is generally agreed, however, that the disseminated, acute type should not be treated with radium or any other radical method. In the chronic, discoid type with thickened patches good results or improvement have been reported by many writers. The effects of treatment, however, are uncertain, for some patients remain well for years; in many the disease soon recurs, and others fail to improve. Most authors advise the use of unfiltered radiation, or of filtration with 0.1 mm. of aluminum for thickened patches, with a dosage sufficient to produce a

7. Pfahler, G. E.: Am. J. Roentgenol. **7**:344 (July) 1920.

fairly sharp reaction, repeated as soon as the reaction has subsided. Simpson employs one fourth strength applicators screened with 0.1 mm. of lead, in half-hour exposures on successive or alternate days, until four or five treatments have been given, and repeats the treatment in about four weeks. It is advised that the normal skin for a distance of from 5 to 10 mm. surrounding the lesion be included in the treatment. In lesions that have been recently treated with iodine or that at any time have been treated with carbon dioxide snow, it is necessary to proceed with caution in the use of radium as they are likely to react out of proportion to the dosage.

The results of radium therapy in lupus vulgaris are such as to indicate that radium has a special field of usefulness in the treatment of small single and multiple patches, recurrent nodules embedded in scar tissue, nodules on the ear and nose, and more especially in lupus of the mucous membranes. A penetrating and destructive type of radiation seems to give the best results. For cutaneous lesions Lewandowsky⁸ advises filtration with 0.1 mm. of lead and a dose sufficiently large to produce necrosis, which is not repeated for from three to four months. In lesions of the mucous membranes he uses tubes, less filtration, and repeats the treatment at shorter intervals, and claims excellent results from this method. Reports of others are not as optimistic, and it has been repeatedly observed that lupus patches when treated with radium heal in the center but extend actively at the periphery in spite of irradiation well beyond the margins.

The prominence that radium has acquired as a therapeutic agent in dermatology is largely due to its effects in the cutaneous conditions discussed above. There are, however, many other dermatologic conditions in which its value is recognized. Among them are the verrucae, and especially the periungual and plantar types, rhinophyma, acne keloid, cheilitis exfoliativa, linear nevi, sarcoid, extramammary Paget's disease, synovial cysts of the skin and others.

Attention has recently been directed to the effect of radium in securing the healing of intractable and indolent ulcers of various kinds. The method is original with Irvine and consists in exposing the edges of the ulcer for from five to ten minutes to the unfiltered rays of a full strength applicator covered with one layer of rubber dam and held in contact. By this means Stokes obtained prompt healing of a granuloma-inguinale type of ulcer that had broken down repeatedly and proved unresponsive to all other treatment, and Oliver secured rapid healing of a similar lesion. I have used this method in two small, indolent trophic ulcers, which healed rapidly after one treatment.

8. Lewandowsky, F.: *Tuberkulose der Haut* (Enzykl. d. klin. Med.), Berlin, J. Springer, 1916, p. 290.

A field of usefulness likewise exists for radium in the treatment of some patches of lichenified eczema and neurodermitis, and of individual lesions of psoriasis and lichen planus.

The introduction of radiotherapeutic agents into dermatologic practice constitutes, perhaps, the most important addition to this field of medicine in many years. The position occupied among these agents by radium is admittedly one of prominence, and in some instances of superiority.

The writer desires to acknowledge his indebtedness to the following authors, whose books have been referred to and quoted in the preparation of this article.

Colwell and Russ, Radium, X-Rays and the Living Cell, London, Bell and Sons, 1915.

Geo. M. MacKee, X-Ray and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea and Febiger, 1921.

Frank E. Simpson, Radium Therapy, St. Louis, C. V. Mosby Company, 1922.

Robert Knox, Radiography, X-Ray Therapeutics, and Radium Therapy, New York, The Macmillan Company.

OCCUPATIONAL HAZARDS OF THE RADIOLOGIST, WITH SPECIAL REFERENCE TO CHANGES IN THE BLOOD ¹

By RUSSELL D. CARMAN, M. D., and ALBERT MILLER, M.D. 1915
Section on Roentgenology, Mayo Clinic, Rochester, Minnesota

THAT the practice of radiology entails certain hazards to health and life was forcibly impressed on its practitioners many years ago, but not until a large number of radiologists had suffered or died from radiodermatitis and cancer. Rolleston says that according to Ledoux-Labard there have been a hundred victims of cancer among radiologists. To this long roll of professional sacrifice is added from time to time the name of some pioneer who sustained his injuries in the early days, but was granted a postponement of the inevitable result. It was soon learned that this danger could be averted by the ordinary precautions which are now habitually employed. So effective are these methods in the prevention of skin lesions that the radiologist has apparently been lulled into a false sense of security from all harm. His serenity is not due to ignorance, but to an unwarranted optimism in the face of his abundant knowledge. He is fully aware that an intact skin may cover a multitude of internal changes wrought by irradiation. These changes are the expected result of radiotherapy; they are found at the necropsy table, are substantiated by experiments on animals, and are demonstrated conclusively by the microscope and the test tube. The literature on deep irradiation effects is overwhelming, both in magnitude and complexity, and the references here appended constitute but a small fraction of the total.

Studies which are almost fascinating in interest have been made of irradiation effects on virtually every organ and tissue of the body, including the digestive tract, blood, bones, heart, lungs, liver, pancreas, eyes, brain, nerves, kidneys, spleen, gonads, and ductless glands. Findings have not always agreed, nor is this surprising

in view of the different conditions under which the tests were made. Notwithstanding discrepancies and contradictions, it is impressive to note that alterations of some sort were found almost constantly, and that in many instances they were produced by moderate or even minute amounts of irradiation.

Among generally accepted facts and theories the following are especially pertinent to the present theme, and will bear repetition, however familiar they may be:

1. Radium and the X-rays produce biologic effects which are essentially alike.

2. These effects vary according to the amount of irradiation, and range from stimulation to destruction (36, 44, 46, 64, 85, 87). Although supported by a great preponderance of evidence, the occurrence of stimulation has been denied by Pordes and others. Holzkecht insists that the X-ray is like curare, and that even in small amounts it is destructive, never stimulative.

3. Cells differ in sensitiveness to irradiation, and certain varieties are especially susceptible. Easy vulnerability of the sperm cells is well established. Lymphocytes, endothelium of blood and lymph vessels, immature cells, and cells in the process of mitosis are highly sensitive.

Susceptibility of the blood and the hematopoietic system to irradiation has been shown convincingly by experiments on animals and by tests of patients and radiologic workers. Levin regards the lymphocyte as the most sensitive cell in the animal organism, and asserts that the greater the square surface of entry of the rays, the more severe is the general effect on the blood. Bécélère found that in some persons even a single application of the rays causes a permanent change. As might be expected from varying technical factors, the experimental re-

sults are not uniform. In general, however, they show that the circulating lymphocytes are increased in number by small doses (41, 55, 77), and decreased in number by large (41, 64, 67). Among radiologic workers there is frequently an increase of lymphocytes, either absolute or relative (1, 7, 24, 58, 78), but with severe or long-continued exposure a reduction may occur (7, 54). The polymorphonuclear count is usually diminished, absolutely or relatively (1, 53, 54, 58, 78), although this may be preceded by an initial increase (76, 84). Marked increase of the eosinophiles has been found in radiologic workers (58, 78, 84, 86). The red cells are more resistant than the white, but restoration is slower (4). Radiologic changes in the erythrocytes run the gamut from a slight increase in number and augmentation of the color-index (1, 15, 30, 84) to diminution and hemolysis by intense doses (29, 60). Most investigators have found hastening of coagulation (44, 47, 57) although the opposite has been reported (65). Reduction of blood pressure is a common finding (15, 58, 88), various alterations of the blood chemistry have been noted (9, 10, 28), and histologic changes in the bone marrow are well-confirmed experimentally (24, 25, 51, 80).

Evidence is increasing that the intestinal mucosa is markedly sensitive. In dogs, Hall and Whipple produced a necrosis of the epithelium lining the intestinal crypts. Mottram observed that very small doses of radiation, less than would be required to affect the testes or skin, altered the production of intestinal mucus. Intestinal ulceration following deep therapy is by no means unknown.

The mooted matter of personal idiosyncrasy has a bearing on hypersensitiveness to radiant energy, and while this factor has perhaps been exploited unduly, it has some basis in fact.

4. Irradiated cells have a lowered resistance to other unfavorable influences, including trauma and possibly certain infections. Moreover, as Loeb has pointed

out, "chain reactions" may occur, one effect giving rise to another, with ultimately severe results.

5. Radiologic workers, so far as they themselves are concerned, are inclined to lay too much stress on the difference in effect of hard and soft rays, and to assume, quite inconsistently, that hard rays, regardless of their aggregate amount, are unlikely to affect the operator. With respect to the skin there is admittedly a difference between hard and soft rays. Martius has shown that rays with a wave length of 0.56 have nearly four times as great an effect as rays with a wave length of 0.325. On the other hand, only hard rays can reach the deeper tissues, and hard rays are in daily use for that purpose. Hall and Whipple found not only that the intestines of dogs were gravely affected by hard rays, but that fatality increased in ratio to the spark gap. Mottram considers it probable that the gamma rays of radium have a destructive action on bone marrow which relatively soft beta rays may not possess. Regaud is cited by Withers as asserting that gamma rays and X-rays of very short wave length are "elective poisons" for nuclear chromatin.

6. The cumulative effect of radiation, which the radiologist guards against so zealously in therapy, cannot be ignored in estimating the chances of injury to himself. Cells affected by the X-rays or radium and re-exposed before sufficient time has elapsed for complete restoration to normal, are altered on an ascending scale, and in the case of hypersensitive cells it is logical to assume that even minute doses frequently repeated may have momentous consequences to their growth and function.

7. By analogy it may be reasoned that radiant energy, like certain drugs, may set up an increase of cellular resistance. This is indicated empirically by the decreasing responsiveness of newgrowths to irradiation. Warren and Whipple have found a suggestion of increased tolerance of dogs to subsequent X-ray exposures. Loeb offers the hypothesis that new cell races

which are more resistant than their ancestors may develop. The fact that many radiologists have been exposed for years, yet survive in apparent good health, is an item of corroboration.

However, the profession cannot safely emphasize the hypothesis of immunization, for there is also evidence that an opposite condition, that of anaphylaxis, may develop in patients. Granting that either immunization or anaphylaxis may occur, the exact circumstances likely to induce one or the other effect are not known.

8. To the foregoing premises is to be added the fact that radiologists are not and cannot be shielded completely from irradiation while pursuing their vocation. Protection can only be relative, and the gamma rays of radium and X-rays of short wave length penetrate ordinary barriers appreciably. The fluoroscopist and the dispenser of radium and high voltage therapy are especially exposed. Even with customary safeguards, some degree of scattered and secondary irradiation is inevitable. Moreover, not all radiologists are scrupulous in the exercise of care, and some of them are daring to the point of recklessness. Admitting that with routine measures of protection the radiologic worker receives only minimal doses, these are repeated day after day through the years. Even if their effect is only stimulative, the results of long-continued stimulation are to be reckoned with.

In view of these data the injuries to radiologic workers which may eventually come to light offer a broad theme for conjecture. But the radiologist, confident of his defense against radiodermatitis, and quite unterrified by the chance of emasculation or lesser damage, waits for absolute proofs that more serious dangers threaten him. Such proofs have begun to appear, and, in consonance with the results of experimental research, lesions of the blood and at least one authentic case of intestinal injury lead the van.

INTESTINAL INJURY

With regard to intestinal injury, only a single case, that of the English radiologist, Barclay, is of sufficient gravity and sufficiently confirmed to warrant recording. After twelve years of work, including much screening without an apron, Barclay had several diarrheic attacks with loss of weight. Mucous casts were noted in the stool on a few occasions. On ceasing work the attacks disappeared in three weeks, and on returning to duty they recurred in from eighteen to twenty days. This cycle was confirmed eight or nine times. Since using additional protection he has been comparatively free from such troubles.

It would be interesting to know whether or not the gastro-intestinal complaints of certain other colleagues have any relation to their occupation. For example, an associate of many years recently had a severe hematemesis and diarrhea, the latter recurring on several occasions. A Western radiologist gives a similar history. In both instances a thorough physical and radiological examination failed to reveal an adequate cause. While no definite relation to irradiation has been established in either case, a systematic study of radiologists from this standpoint might develop valuable information.

FATALITIES FROM DISEASE OF THE BLOOD

No less than six deaths from aplastic anemia have occurred among radiologic workers.

The first, a classic and oft-repeated story, was that of Dr. Tiraboschi (18), an Italian roentgenologist, who, after fourteen years' service with little or no means of protection, died of a "profound essential anemia" in 1914. Three years prior to this he had a severe nervous breakdown, but was able to resume his duties after six months. Although he showed an increasing pallor and complained of loss of strength his nutrition was good, and he continued to work until his death. Among other abnormalities, necropsy revealed extreme testicular atro-

phy, diminution and hardening of the spleen, and pronounced alterations in the marrow of the ribs.

Next in chronologic sequence were the three cases in radium workers reported by Mottram (53) in 1920. One of these, a woman aged thirty-six years, had been engaged in the work for eight years, during which time she was in excellent health. Pallor developed after a holiday of two months. Her red cell count and hemoglobin progressively diminished; there was definite leukopenia and anisocytosis, and death occurred after seventy-three days. Another was a man aged thirty-three years, a worker with radium for three years. He, too, was taken ill after a month's holiday, and the blood picture was similar to that in the preceding case. Death ensued after three months. The last case of the trio was a man aged fifty years who had worked with radium for ten years. His fatal illness was of short duration. The diagnosis of aplastic anemia was supported by the blood findings.

Dr. Ironside Bruce, of England, was the fifth victim (40). Bruce was in his early forties, and had been engaged in radiology for about eighteen years. He was of good physique, had lately gained in weight, and his general health was never better. In October, 1920, a blood count, made quite accidentally, showed a slight diminution of the red cells and hemoglobin. From that time until his death, in March, 1921, the red cells, hemoglobin and white cells steadily diminished. Low blood pressure, a relative lymphocytosis and a poikilocytosis were other features.

The sixth death recorded was that of Dr. Nordentoft (24), a Danish radiologist who had employed X-ray therapy for twelve years and was not always careful in taking precautions. Some years ago he noted testicular atrophy. In November, 1921, he complained of fatigue, and an examination of the blood disclosed a slight reduction of the red and white cells. Several months later he again became weak and dyspneic. At this time diminution of

red cells was marked: anisocytosis, microcytosis and poikilocytosis were also pronounced. Demoralization of the blood picture rapidly became extreme, and he died within another month.

Dr. F. M. Sylvester, of Oak Park, Illinois, writes the following interesting letter:

"About two years ago, I was doing some research work towards the establishment of a so-called lethal cancer dose. At this time I was working with a kilovoltage varying from 160 to 280. My protection consisted of a booth of one-inch pine covered with one-eighth inch lead and quarter-inch beaver board. This booth was completely covered, with the exception of the floor, which had no protection. The booth was approximately eight feet from the tube. I was spending on an average of four hours an evening in this booth, with the tube in constant operation during this time.

"The first manifestation of illness was the usual tired, weary sensation. As these symptoms became more pronounced, I naturally suspected the X-ray, and made several tests around through other parts of my laboratory to see if I was getting irradiation either from radium or from other machines. These tests proved negative to such an extent that I felt satisfied that there was perhaps another cause. In the meantime an anemia developed, the red count dropping from 5,200,000 to less than 4,000,000. I now made several tests with an iontoquantimeter within the booth, and found that radiation was coming in through the floor. In fact, this was to such an extent that an eight by ten film could be fogged in eight minutes' time operating with a kilovoltage of anything above 200 k.v. I immediately had the floor of the booth covered, and at Dr. Darnell's suggestion, walled off a room, and covered the same with one-eighth inch lead. This room was utilized for the patient, thereby giving me a protection of the one-eighth inch lead on the booth, as well as the one-eighth inch lead in the treatment room.

"I now found, on tests, that there was no further evidence of perceptible radiation. The damage, however, in my case had been done, and the red count dropped to 2,500,000. At this time I was confined to my bed and my life despaired of. Relative to blood changes, there were several things of interest that we noted. The blood pressure, which normally had been 130 systolic, fell to 105. (This, by the way, has never come back beyond 110.)

"The alkaline reserve at the beginning showed a relative increase. This gradually fell, as you can see by enclosed charts, and has never returned to a normal point."

Six blood counts made between June 15 and August 21, 1922, tell a graphic story of Dr. Sylvester's illness, and are tabulated herewith:

punctilious as to protection and sometimes omitted wearing an apron. During the last year he complained of extreme exhaustion at the end of the day's work. Early in

TABLE 1

DATE	JUNE 15	JUNE 29	JULY 5	JULY 18	JULY 28	AUG. 21
Erythrocytes	5,200,000	3,900,000	3,000,000	2,500,000	3,500,000	4,200,000
Leukocytes	8,000	6,500	5,000	8,000	7,000	8,000
Hemoglobin %	80	65	55	41	61	70
Color index	1.25	1.00	1.09	1.21	0.84	1.14
Coagulation time	4 min.	3 min.	2.5 min.	5 min.	4 min.	3 min.
Erythrocytes						
Color	normal	pale	pale	pale	pale	pale
Size	normal	small	small	small	small	normal
Shape	normal	crenated	crenated	crenated	oval	oval
Poikilocytes	0	+	+	+	0	0
Polychromatophilia	0	+	++	++	0	0
Basophile granulation	0	0	0	+	0	0
Microcytes	0	+	+	+	+	0
Macrocytes	0	0	0	0	0	0
Microblasts	0	0	+	+	0	0
Normoblasts	0	+	0	0	0	0
Megaloblasts	0	0	0	0	0	0
Howell's Particles	0	0	0	+	0	0
Lymphocytes						
Sm. mononuclear %	27	30	30	14	24	23
Lg. mononuclear %	6	8	14	10	8	10
Transitionals %	2	0	0	0	0	0
Neutrophiles						
Mononuclear %	0	0	0	0	0	0
Polynuclear %	63	60	54	70	65	56
Eosinophiles %	1	2	2	3	3	1
Myelocytes %	0	0	0	0	0	0
Basophiles %	1	1	0	3	0	0
Mast cells %	0	0	0	0	0	0
Free nuclei %	0	0	0	0	0	0
Alkaline reserve %	7.6	7.8	6.4	6.1	7.0	7.3
Hydrogen-ion %	6.3	6.2	6.1	6	6.3	6.7

LYMPHATIC LEUKEMIA

The chief stimulus for reviewing this subject was the recent death of Dr. Walter Mills, of St. Louis. Dr. Mills was forty-six years old and had been engaged in clinical roentgenology of the digestive tract for about fourteen years. The volume of his work was large and consisted chiefly of

1924 a blood count, made casually, showed signs of a lymphatic leukemia. Shortly afterward he discovered some swelling of the cervical and inguinal lymph nodes. He came to the Mayo Clinic in February and the existence of the leukemia was confirmed. Blood counts, details of which are tabulated herewith (Table 2), revealed

of which were lymphocytes. The red cells numbered 4,220,000 to 4,600,000 and the hemoglobin was 65 to 70 per cent.

TABLE 2

	FEBRUARY 4	FEBRUARY 6
Hemoglobin, %	70	65
Erythrocytes, millions	4.60	4.22
Leukocytes	25,800	30,400
Lymphocytes, %	96.5	96.5
Neutrophils	2.0	3.5
Platelets	240,000	310,000
Anisocytosis	slight	slight
Poikilocytosis	slight	slight
Polychromatophilia	slight	slight
Coagulation time (Bogg)	6 minutes	

Shortly after coming to the Clinic, Dr. Mills developed appendicitis, and operation became imperative notwithstanding the unfavorable circumstances. Death followed three days later.

Various interpretations of Mills' case are obvious. Exposure to the X-rays may have had no causative relation to the leukemia. Indeed, the X-rays may have mitigated the disease. On the other hand, the X-rays are capable of causing malignant lesions of the skin and may have induced this malignancy of the blood. Further, Mills' father died from cancer, so that the hereditary factor, emphasized by Slye, was present. At all events, the case is worthy of publicity for future consideration.

Only two references to a possible relation between exposure to irradiation and lymphatic leukemia were discovered in the literature. One was a statement in 1911 by von Jagic and his collaborators, as follows: "Several years ago a Vienna roentgenologist died of lymphatic leukemia. At the same time it was announced that a practicing roentgenologist of Munich had passed out with the same disease. One of us (Schwarz) had the opportunity of observing a case of leukemia in a chemist who had been occupied for a long time in

the production of radium. Recently we have received the news that an American roentgenologist had also fallen a victim to this disease." Unfortunately, von Jagic gives no specific details, and the identity of the American roentgenologist referred to is unknown to us. However, his language is declarative regarding two of the cases, and is entitled to credence. In a late paper, Amundsen (24) states that the lymphocytes of radiologic workers are regenerated very rapidly, and the over-production may be regarded as an attempt to compensate for the leukopenia. Hence, he says, "the cases of lymphatic leukocythemia that are reported as having occurred among radiologists may no doubt be interpreted as a lymphocytic regeneration overshooting the mark."

In this connection, it might be pointed out that deaths of radiologists are often reported without any information as to the cause. For the welfare of the profession, it is to be hoped that in future the records of all such deaths will be given in detail, and with due attention to the occupational phase.

INJURIES AND FATALITIES FROM ELECTRIC CURRENTS

Besides the effects of radio-activity, the roentgenologist is exposed to another hazard, that of electric shock. Rare, indeed, is the roentgenologist who has not witnessed or been the target of such shocks. Fatalities to patients have happened, and records of most of these can be found in the annals of medical jurisprudence. The death of Dr. Jaugeas, December 2, 1919, (13) should not be difficult to recall. Dr. Clatus Cope, a dentist of Seymour, Indiana, was electrocuted July 16, 1920. Doubtless this list is not complete, for personal accidents are not indexed as carefully as scientific papers.

THE PERSONAL EQUATION

Injuries and fatalities to radiologists from cancer, aplastic anemia, lymphatic leukemia and electric shock thus assume

considerable proportions. The reaction of the profession to them will be determined by the personal equation. The optimist and the pessimist can each find strong arguments in the whole array. In the one view, dermatitis and cancer belong to ancient history, irradiation has not been proved with mathematical precision to be a cause of aplastic anemia or lymphatic leukemia, and accidents are always possible to those who work with electric currents. In the other view, radio-activity is so dangerous that its employment should be left entirely to those who are willing to assume the most extraordinary risks.

As usual, the truth is probably between these extremes. In that case, the optimists, who seem to be in the majority, must be roused to a proper sense of their unnecessary jeopardy. Fear that the eligibility of radiologists for life insurance might be impaired by too much publicity has perhaps inspired a certain modesty of opinion in the past. But this attitude is shortsighted, for with open recognition of his perils the radiologist will employ more effective means to avert them.

PREVIOUS WARNINGS

Warnings of hidden dangers to radiologists have not been lacking. Von Jagic and his associates made examinations of several roentgenologists in 1911 and showed that blood changes had occurred. Portis published the results of similar tests in 1915. Later, the deaths of Tiraboschi and Bruce were made the occasion of urgent admonition by editorial writers. Five years ago Mottram began to write extensively for the benefit of radium workers, and his efforts were seconded by Pinch. In 1920 and again in 1921, de Courmelles emphasized the gravity of the situation. In 1922, Cafaratti, Amundsen and Pfahler each gave serious attention to the subject of hematic changes in radiologists. Last year Faber reported the death of Nordentoft, and again cautioned other workers. Hemler, in 1922, and Shearer, in 1923, wrote of the

hazard from electric shock and the methods of avoidance.

Pfahler's paper deserves more than passing mention. He canvassed the radiologists of America to learn whether they were sustaining hematic changes or other injury, and received many replies. In general, the professional workers had a slight leukopenia and a relative increase of lymphocytes. A few had an increase of eosinophiles. Twelve had delayed clotting of the blood. Systolic blood pressure was decreased, as a rule. While in most instances the changes in the blood picture were only slightly beyond normal limits, Pfahler regarded them as probably significant of excessive irradiation and as danger signals. In the main, nurses and lay assistants seemed intact, but ten of them had blood changes or other abnormalities, or were receiving excessive exposure. Many of the roentgenologists reporting to Pfahler complained of marked fatigue from their work, but Pfahler believes that similar fatigue would follow equal activity in other occupations. It is noteworthy, however, that radium workers have also complained of fatigue.

PREVENTION OF INJURY

Viewing all this evidence, even in the most liberal light, the conclusion is inescapable that many radiologists are being harmed in their daily work and are menaced by graver injuries. To avert these injuries it is necessary, first of all, that the radiologic worker be impressed so thoroughly with his danger that he will take adequate precautions. Either the methods of protection now in common use are not effective, or the worker is careless in their application. As Pfahler and others have said, not only the means of protection but the will to use it is requisite.

It is needless here to review protective measures at length, for the principles are familiar and easily applied. It might be emphasized, however, that the worker should be shielded not only from direct rays, but also from secondary irradiation

which may reach him from any angle. For the radiographer efficient protection can be secured by simple means, but in fluoroscopy and radiotherapy more elaborate measures are required. Protection from irradiation and prevention of electric shocks have been given more attention of late by the manufacturers of X-ray apparatus.

Even with all practicable safeguards, a certain degree of exposure cannot be evaded. Laboratories doing a large volume of work should, therefore, have a reserve personnel to permit alternation of service or frequent holidays. Workers should repeatedly be cautioned to receive the least possible amount of irradiation consistent with the performance of their duty. Modern life, regardless of occupation, has an abundance of risks, and additions are superfluous. Besides taking all reasonable precautions, workers should have frequent medical examinations.

One of the first maxims learned by the physician is "*non nocere*" (harm not), and he is seldom faithless to it with regard to his patients. Is his own body less worthy of care?

BIBLIOGRAPHY

1. AMUNDSEN, P.: The blood picture of radiologists. Tidsskrift for den Norske Laegeforening, 1922, 862. Abst., Jour. Roentgen Soc., 1923, XIX, 25.
2. AMUNDSEN, P.: Blood anomalies in radiologists and in persons employed in radiological service. Acta Radiologica, 1924, III, 1-7.
3. BARCLAY, A. E.: A danger of the Coolidge tube for screen work. Editorial, Arch. Radiol. and Electroth., 1921, XXV, 225-227.
4. BECLERE, M.: Que doit-on espérer et que peut-on craindre de l'emploi, en radiothérapie profonde, de rayons très pénétrants. Arch. d'électr. méd., 1921, XXXI, 225-237.
5. BORDIER, H.: Biochemische Strahlenwirkung mit besonderer Berücksichtigung der Roentgenstrahlen. Fortschr. a. d. Geb. d. Roentgenstrahlen, 1913, XX, 202-220.
6. BORDIER, H.: Sur un cas d'anémie mortelle. Bull. et mém. Soc. radiol. méd. de France, 1921, IX, 158-160.
7. CAFFARATTI, M.: Quantitative Veraenderungen der Blutelemente bei Roentgenologen und Personal in Roentgen Instituten. La Radiol., Medica, August, 1922. Abst., Fortschr. a. d. Geb. d. Roentgenstrahlen, 1923, XXX, 382.
8. CONTREMOULINS, M. G.: A propos de la protection des tiers contre les rayons X. Arch. d'électr. méd., 1921, XXXI, 314-315.
9. CORI, C. F.: Biological reaction of X-rays: The influence of X-ray treatment on the complement content of the blood of cancer patients. Am. Jour. Roent. and Rad. Ther., 1923, X, 830-834.
10. CORI, C. F., and PUCHER, G. W.: Biological reactions of X-rays: Effect of radiation on the nitrogen and salt metabolism. Am. Jour. Roent. and Rad. Ther., 1923, X, 738-745.
11. CUMBERBATCH, E. P.: Fatal leucopenia following X-ray treatment. Arch. Roentg. Ray, 1913-1914, XVIII, 187.
12. DAVID, O., and HIRSCH, A.: Experimental studies on the adrenalin content of the suprarenals following roentgen irradiation. Klin. therap. Wchnschr., 1923, 790. Abst., Am. Jour. Roent. and Rad. Ther., 1923, X, 1010.
13. DE COURMEILLES, F.: Accidents des rayons X et du radium. Arch. d'électr. méd., 1921, XXXI, 289-298.
14. DE COURMEILLES, F.: Hygiène et sécurité du radiologue. Radiopathie et radiothérapie. Arch. d'électr. méd., 1920, V, 177-186.
15. DESJARDINS, A. U., and MARQUIS, W. J.: Blood count and blood pressure in high voltage therapy. Radiol., 1924, II, 252-259.
16. DESJARDINS, A. U.: Protection against radiation. Radiol., 1923, I, 221.
17. DESSAUER, F.: The cause of the action of X-rays and gamma rays of radium upon living cells. Jour. Radiol., 1923, IV, 411; also Strahlentherapie, 1923, XVI, 208. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 122.
18. EDITORIAL: The autopsy of a radiologist. Arch. Roentg. Ray, 1914, XVIII, 393-394. (Data from La Radiologia Medica, February, 1914.)
19. EDITORIAL: Arch. Radiol. and Electroth., 1921, XXV, 338-339.
20. EDITORIAL: Arch. Radiol. and Electroth., 1921, XXV, 193-194.
21. EDITORIAL: Arch. Radiol. and Electroth., 1920, XXIV, 341.
22. EDITORIAL: The dangers in working with radium and X-rays. How the problem is being met. Radium, 1921, XVII, 53-60; London Correspondent of Jour. A. M. A., 1921, LXXXVI, 1412.
23. ENGEL, K.: Ueber Roentgenschädigungen in der medizinischen Radiotherapie. Deutsch. med. Wchnschr., 1907, XXXIII, 22-24.
24. FABER, K.: Anémie perniciose aplastique mortelle chez un spécialiste des rayons roentgen. Acta Radiologica, 1923, II, 110-115.
25. FRAENKEL, E., and BUDDE, W.: Histologische, zytologische und serologische Untersuchungen bei roentgenbestrahlten Meerschweinchen. Fortschr. a. d. Geb. d. Roentgenstrahlungen, 1913, XX, 355-363.
26. FALCONER, E. H., MORRIS, L. M., and RUGGLES, H. E.: The effect of X-rays on bone marrow. Am. Jour. Roent. and Rad. Ther., 1924, XI, 342-351.
27. GIRAUD, M., GIRAUD, G., and PARES, G.: La crise hémoclasique du mal des irradiations pénétrantes. Presse méd., 1921, XXIX, 746-748.
28. HALL, C. C., and WHIPPLE, G. H.: Roentgen-ray intoxication; disturbances in metabolism produced by deep massive doses of the hard roentgen rays. Am. Jour. Med. Sc., 1919, CLVII, 453-482.
29. HAUSMANN, W., and KERL, W.: Zur Kenntniss der biologischen Radiumwirkung. Strahlentherapie, 1921, II, No. 3. Abst., Fortschr. a. d. Geb. d. Roentgenstrahlen, 1921-1922, XXVIII, 275.

30. HEIM, K.: Blut Veraenderungen bei der Grossfelderbestrahlung. Arch. f. Gynaek., 116, II, 291. Abst., Fortschr. a. d. Geb. d. Roentgenstrahlen, 1923, XXX, 613.
31. HEMLER, W. F.: High tension electric shocks in roentgenologic practice. Am. Jour. Roent., 1922, IX, 365-370.
32. HENKEL, M., and GUEFFROY, H.: Blutgerinnung bei Tiefentherapie. Zentr. f. Gynaek., 1923, No. 11. Abst., Fortschr. a. d. Geb. d. Roentgenstrahlen, 1922, XXIX, 534.
33. HIRSCH, E. F., and PETERSEN, A. J.: The blood with deep roentgen-ray therapy; hydrogen-ion concentration, alkali reserve, sugar and non-protein nitrogen. Jour. Am. Med. Assn., 1923, LXXX, 1505-1507.
34. HOLZKNECHT, G.: Gibt es ein Reizwirkung der Roentgenstrahlen? Muenchen. med. Wchnschr., 1923, LXX, 761-762.
35. HUSSEY, R. G., and THOMPSON, W. R.: The effect of radium emanations on solutions of trypsin. Jour. Radiol., 1923, IV, 260.
36. IVY, A. C., ORNDORFF, B. H., JACOBY, A., and WHITLOW, J. E.: Studies of the effect of X-rays on glandular activity. Jour. Radiol., 1923, IV, 189-199.
37. KLEIN, J.: The rapidity of sedimentation of erythrocytes before and after roentgen irradiation. Strahlentherapie, 1923, XVI, 233. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 128.
38. KROENIG, B., and FRIEDRICH: The principles of physics and biology of radiation therapy. London, W. Heinemann, Ltd., 1922. Review in Arch. Radiol. and Electrother., 1922-1923, XXVII, 216-217.
39. LACASSAGNE, A., and LAVEDAN, J.: Histologic modifications of the blood after experimental radiations. Paris méd., 1924, XIV, 97. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 269-270.
40. LARKINS, F. E.: A case of acute aplastic anemia. Arch. Radiol. and Electrother., 1921, XXV, 380-382.
41. LAZARUS-BARLOW, W. S.: Some biological effects of small quantities of radium. Arch. Radiol. and Electrother., 1919-1920, XXIV, 1-12.
42. LEITSCH, A.: The immediate effects of X-rays on the blood lymphocytes. Arch. Radiol. and Electrother., 1921-1922, XXVI, 122-128.
43. LEVIN, I.: Action of radium and the X-rays on the blood and blood-forming organs. Am. Jour. Roentgenol., 1922, IX, 112-116.
44. LEVY-DORN, M., and WEINSTEIN, S.: Zum Verhalten des Blutdrucks nach Roentgenbestrahlung. Fortschr. a. d. Geb. d. Roentgenstrahlen, 1921-1922, XXVIII, 175-178.
45. LITTLE, C. C., and BACC, H. J.: The occurrence of two heritable types of abnormality among the descendants of X-rayed mice. Am. Jour. Roent. and Rad. Ther., 1923, X, 975.
46. LOEB, L.: The effects of roentgen rays and radioactive substances on living cells and tissues. Am. Jour. Roentgenol., 1922, XIV, 497-498.
47. MAHNERT, A., and ZACHERL, H.: The influence of roentgen rays on the body fluids and metabolism of the human organism. Strahlentherapie, 1923, XVI, 163. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 125.
48. MARTIUS: The biological effects of X-rays of different wave lengths. Strahlentherapie, XIV, 558. Abst., Arch. Radiol. and Electrother., 1922-1923, XXVII, 382.
49. MARTIUS: Experimental studies of the action of roentgen rays. Arch. f. Gynaek., 1923, CXX, 193. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 124.
50. MAVOR, J. W.: Studies on the biological effects of X-rays. Am. Jour. Roent. and Rad. Ther., 1923, X, 968-974.
51. MOTTRAM, J. C.: Histological changes in the bone marrow of rats exposed to the gamma radiations from radium. Arch. Radiol. and Electrother., 1921, XXV, 197-199.
52. MOTTRAM, J. C.: Some effects of exposure to radium upon the alimentary canal. Arch. Radiol. and Electrother., 1923, XXVIII, 28-31.
53. MOTTRAM, J. C.: The red cell blood content of those handling radium for therapeutic purposes. Arch. Radiol. and Electrother., 1920, XXV, 194-197.
54. MOTTRAM, J. C., and CLARKE, J. R.: The leukocytic blood content of those handling radium for therapeutic purposes. Arch. Radiol. and Electrother., 1919-1920, XXI, V, 345-350.
55. NAKAHARA, W.: Studies on X-ray effects. III. Changes in the lymphoid organs after small doses of X-rays. Jour. Exper. Med., 1919, XXIX, 83-87.
56. NAKAHARA, W., and MURPHY, J. B.: Studies on X-ray effects. The biological action of small doses of low frequency X-rays. Jour. Exper. Med., 1922, 475. Abst., Jour. Radiol., 1922, III, 251.
57. PACNIEZ, RAVINA, and SOLOMON: Action des rayons de Roentgen sur la coagulation du sang. Bull. et mém. Soc. radiol. méd. de France, 1921, IX, 256-258.
58. PFAHLER, G. E.: The effects of the X-rays and radium on the blood and general health of radiologists. Am. Jour. Roentgenol., 1922, XIV, 647-656.
59. PICCALUCA, N.: The action of roentgen rays on the reducing capacity of normal tissue and of newgrowths. Strahlentherapie, 1923, XVI, 245. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 125.
60. PINCH, A. E. H.: A report of the work carried out at the Radium Institute from January 18, 1919, to December 31, 1919. Arch. Radiol. and Electrother., 1920, XXV, 50-62.
61. PORDES, F.: In explanation of the action of X-rays is it necessary to assume functional and growth stimulation? Arch. Radiol. and Electrother., 1923, XXVIII, 89-93.
62. PORTIS, M. M.: Blood changes in workers with the roentgen ray, and apparatus for protection. Jour. Am. Med. Assn., 1915, LXV, 20-21.
63. RISSE: Some blood changes during roentgen and radium action. Arch. f. Gynaek., 1923, CXX, 181. Abst., Internat. Survey Roent. and Radiother., 1924, VII, 127.
64. ROLLESTON, H.: Acute constitutional symptoms due to radiation. Jour. Roentgen Soc., 1923, XIX, 5-18.
65. RUSS, S.: The immediate effects of X-rays on the blood lymphocytes. Arch. Radiol. and Electrother., 1921-1922, XXVI, 146-149.
66. RUSS, S., CHAMBERS, H., and SCOTT, G. M.: The local and generalized action of radium and X-rays upon tumor growth. Arch. Radiol. and Electrother., 1921-1922, XXVI, 129.
67. RUSS, S., CHAMBERS, H., and SCOTT, G. M.: Further observations of the effects of X-rays upon lymphocytes. Arch. Radiol. and Electrother., 1921, XXV, 377-380.

68. RUSS, S., CHAMBERS, H., SCOTT, G. M., and MOTTRAM, J. C.: Experimental studies with small doses of X-rays. *Lancet*, 1919, CXCVI, 692-695.
69. SCHALL, W. E.: The stimulating and paralyzing effect of X-rays. *Arch. Radiol. and Electrother.*, 1923, XXVIII, 124-125.
70. SHEARER, J. S.: Possible dangers in connection with the use of the X-rays and how to avoid them. *Am. Jour. Roent. and Rad. Ther.*, 1923, X, 240-246.
71. SIMONS, A.: Experimenteller Beitrag zum Problem der Wachstumsteigernden Wirkung der Roentgenstrahlen auf normales menschliches Gewebe. *Fortschr. a. d. Geb. d. Roentgenstrahlen*, 1923, XXX, 300-301.
72. SLYE, M.: The inheritability of spontaneous cancer in mice and its application to cancer in man. *Jour. Radiol.*, 1922, III, 453-464.
73. SOILAND, A.: Protection to the operator from unnecessary radium radiation. *Jour. Radiol.*, 1922, IX, 683.
74. STRAUSS, O.: The effect of roentgen rays on intracellular and metabolic processes. *Strahlentherapie*, 1923, XVI, 195. Abst., *Internat. Survey Roent. and Radiother.*, 1924, VII, 126.
75. STRAUSS, O.: Different degrees of sensitiveness to roentgen rays. *Fortschr. a. d. Geb. d. Roentgenstrahlen*, 1924, XXXI, 428. Abst., *Internat. Survey Roent. and Radiother.*, 1924, VII, 271.
76. TAYLOR, H. D., WITHERBEE, W. D., and MURPHY, J. B.: Studies on X-ray effects. I. Destructive action on blood cells. *Jour. Exper. Med.*, 1919, XXIX, 75-82.
77. THOMAS, M. M., TAYLOR, H. D., and WITHERBEE, W. D.: Studies on X-ray effects. II. Stimulative action of the lymphocytes. *Jour. Exper. Med.*, 1919, XXIX, 75-82.
78. VON JAGIC, N., SCHWARZ, G., and VON SIEBENROCK, L.: Blutbefunde bei Roentgenologen. *Berl. klin. Wchnschr.*, 1911, XLVIII, 1220-1222.
79. VON MIKULICZ-RADECKI, J.: Roentgen irradiation and rapidity of sedimentation of blood corpuscles. *Arch. f. Gynaek.*, 1923, CXX, 187. *Strahlentherapie*, 1923, XVI, 223. Abst., *Internat. Survey Roent. and Radiother.*, 1924, VII, 128.
80. WARREN, S. L., and WHIPPLE, G. H.: Roentgen-ray intoxication. *Jour. Am. Med. Assn.*, 1923, LXXXI, 1673-1675.
81. WARREN, S. L., and WHIPPLE, G. H.: Roentgen-ray intoxication. II. The cumulative effect or summation of X-ray exposures given at various intervals. *Jour. Exper. Med.*, 1923, XXXVIII, 725-730.
82. WARTHIN, A. S.: The changes produced in the kidneys by roentgen irradiation. *Am. Jour. Med. Sc.*, 1907, CXXXIII, 736-746.
83. WARTHIN, A. S.: An experimental study of the effects of roentgen rays upon the blood-forming organs, with special reference to the treatment of leukemia. *Internat. Clin.*, 1906, s. XV, IV, 243-277.
84. WESTMAN, A.: Alterations du sang chez les malades traités par les rayons X et par le radium. *Acta Radiologica*, 1921-1923, I, 349-357.
85. WICKHAM, L.: Modifications histologiques produites par les rayons X sur les tissus. *Arch. d'electr. méd.*, 1913, XXII, 433-447.
86. WINTZ, H.: Injuries from roentgen rays in deep therapy. *Am. Jour. Roent. and Rad. Ther.*, 1923, X, 140-147.
87. WITHERS, S.: Certain biological principles of radiation therapy. *Am. Jour. Roent. and Rad. Ther.*, 1923, X, 776-781.
88. WOLMERSHAUSER, O.: The behavior of blood pressure and leukocytes during roentgen irradiation and their relation to the vegetative nervous system. *Strahlentherapie*, 1923, XVI, 235. Abst., *Internat. Survey Roent. and Radiother.*, 1924, VII, 129.

DISCUSSION

DR. H. J. ULLMANN (Santa Barbara):

Reference was made to a statement by Hall and Whipple regarding the decreased lethal dose when a longer "gap" was used. If one will refer to this article, square the gaps and compare with the lethal doses, he will find that the doses are inversely proportional to these squares. The authors were evidently not familiar with the physical laws governing X-ray output when they assumed that rays generated by a higher voltage were more lethal, for no allowance is made for the increased intensity produced by this increased voltage. When such an allowance is made no difference in the lethal effect is found.

DR. ALBERT SOILAND (Los Angeles):

I believe that Dr. Carman's paper should be given great thought and consideration. There is no one phase of the work we are doing that is more important to us, both physically and from a medico-legal aspect, than protection—and that means not only to ourselves and our technicians, but to the patients we undertake to treat or examine. I have presented this subject on former occasions and am always glad of an opportunity to reiterate, because I believe it is the most important radiological subject we have to deal with to-day. Many years ago, when Dr. Carman was even younger than he is to-day and I used to visit him, I found him sitting behind his fluoroscope, with his bare hands palpating many patients daily. Also, many years ago when Dr. James T. Case was young and handsome, he was doing his fluoroscopic work on the overhead table, which he assumed was fully protected. On one visit I took his fluoroscope and walked around the table with it and had no difficulty in observing the leg bones of Dr. Case as he stood over the table. However, I see that he is still alive and I guess he is

now keeping out of harm's way. In New York last week I saw something which bordered on sheer neglect. I went to one of the large hospitals where deep therapy was being done by someone who is highly intelligent and, I presume, knows every detail of the work. He was operating two high voltage tubes in rooms where open wooden doors with no lead protection permitted the attendants and waiting patients to absorb whatever direct and scattered radiation came their way. In the light of present-day knowledge of the biologic reactions to radiation, this is inexcusable. We should all take to heart what Dr. Carman has said and impress upon ourselves the necessity of protection against every form of unnecessary radiation.

DR. G. E. PFAHLER (Philadelphia): I want to emphasize what Dr. Carman and Dr. Soiland and Dr. Ullmann have said. There is nothing so important to us to-day, and really so important to the advancement of this science, as this question of protection. We must not, on this question of protection, limit ourselves entirely to the roentgenologist, but extend our consideration to the patient. These high voltage machines that are being distributed through the country and installed in some of the hospitals, without the thought of even having a technician do the work, without the supervision of a trained radiologist, make those of us who know the dangers very fearful. We must not imagine that we get protection, especially from these high voltage rays, by simply standing an alleged screen up in front of us. I tried this out very thoroughly in my own laboratory,—not with a screen but by the following process. I placed my high voltage tube under a concrete floor sixteen inches thick; I covered the top of the concrete floor with a quarter of an inch of lead; the only communication from the basement was a small door, and one had to pass around the hallway in order to get up. I thought that that would give protection, because the only rays that came to the room were the beams

of rays that passed through the patients. We soon learned, however, that we had rays not only all over this room but in the neighboring rooms, and we did not get protection until we leaded all of the rooms and doors about the space in which we had only a column of rays coming through. When I see, as we all can see, deep therapy equipment with simply a glass bowl around the X-ray tube, and see patients and physicians and assistants walking around this glass bowl, assuming that they have protection, it just makes one shudder. As Dr. Soiland has well said, a wooden door is no protection,—you must have the leaded wall complete to the ceiling and all the air shut off, because the air itself will carry this radiation through to the adjoining room.

Now test yourselves, as I suggested in my paper to which Dr. Carman kindly referred. Put some dental films in the place where you are standing, and leave them there for a time until you think they are fogged, and test it out. Carry a dental film in your pocket and see how long you can carry it until it becomes fogged. You would be surprised at yourself, when you are working around either radium or X-rays, no matter how careful you are. Then make further tests by examining your blood from time to time.

All these things furnish indices of danger. We must all be more careful, not only in protection against the rays, against the electrical dangers, but also in getting sufficient rest, for we are adding to this over-exhaustion the intense work we are doing, and we must overcome the products of waste in our body plus this radiation effect.

DR. L. T. LEWALD (New York): I think that each laboratory should be inspected according to the regulations of the Board of Health in New York City.

The Board needs support just like this, however, for there is the other side to it: a physician claims, by right of his license, that he can use *any* means *he* sees fit to treat patients, and we have to prove that he

has not that right, for the public must be protected, and even the individual himself. The Board needs your support of the code recently passed, and if New York City goes into court on this problem, as it might on a case such as Dr. Soiland has mentioned, it will have to be tried out. The orders of the Board can be carried out under the police regulations of the city, and the only stumbling block is the question of whether we are going to have the support of the medical profession itself. When it comes to a question as to what the Board of Health may adopt as a standard for adequate protection, we might insist upon these suggestions which were made to-day, which will be brought to the attention of the New York Board of Health. For any violation of the code, even though a laboratory has a license, that license may be revoked. I am sure we will have the support of the court in this matter, if we have the support of the profession. The New York City Code governing this matter follows:

X-RAY LABORATORIES REGULATED

At a meeting of the Board of Health of the Department of Health of New York City, held January 26, 1922, the following resolution was adopted:

Resolved, That Article 7 of the Sanitary Code be amended by adding thereto a new section to be numbered 107, to read as follows:

Section 107. No person shall maintain, operate or conduct an X-ray laboratory or advertise or hold out to the public that an X-ray laboratory is maintained, operated or conducted, wherein radiographs are taken, diagnoses made or human beings

examined or treated by X-rays, without a permit therefor issued by the Board of Health, or otherwise than in accordance with the terms of said permit and with the Regulations of the said Board.

Regulation 3. Precautions against danger.—Every X-ray laboratory shall be so constructed as to confine within the operating room the rays emanating from the machine and it shall be equipped with suitable and necessary appliances and devices at all times when the X-ray machine is in operation for the proper protection of patients, operators and all other persons or property adjacent, contiguous to or coming in contact with the electrical or other current or force or spark generated or incident to the operation and use of the X-ray machine.

Regulation 4. Permits may be revoked in the discretion of the Board of Health.

DR. J. D. SOUTHARD (Fort Smith, Ark.): It seems to me this is one of the most important questions we can possibly consider, and as I have listened to the discussions of the leaders in our profession, giving their experience, it has occurred to me that we ought to at least appoint here at this time, a committee of three men, such as Dr. Carman, Dr. Soiland, and Dr. Pfahler, to formulate something like a minimum of precaution to be taken by every one in the work that we are doing—something as easily practicable and simple as possible—and submit it to this association and let it be published, and then that we all should resolve in our own minds that we will comply with it. I am a new member and do not know whether anything of this kind has been or is being done or not.

THE TREATMENT BY RADIATION OF CANCER OF THE RECTUM*

BY HARRY H. BOWING, M.D., AND FRANK W. ANDERSON, M.D.

Section on Radium and Roentgen-Ray Therapy, Mayo Clinic

ROCHESTER, MINNESOTA

I WAS asked by the Program Committee of this Association to present a paper on the end-results of treatment by radiation of cancer of the rectum. After considering the matter, I decided that statistical data of value could not be obtained in so short a time. Moreover, the topic was being investigated in the Clinic from the surgical standpoint. I decided, therefore, to confine my discussion chiefly to a description of the technique as it is used in the Mayo Clinic.

Da Costa, before a recent meeting of the American College of Surgeons, said that in his experience, radium relieved pain, and that in certain cases in which the growth seemed hopeless, it did give hope. He expressed the belief that radium, used with the knife, with sound clinical judgment, could be recommended as a valuable adjunct, but that a physician who uses radium for all cases is as much a menace to the public as the physician who uses strychnin or the roentgen rays for all diseases.

Recently, W. J. Mayo mentioned that he is favorably impressed with the results of a combination of surgery and radiation in the therapeutic management of rectal carcinoma. He recalled several inoperable cases which became operable following radium exposures, and deplored the fact that many physicians are giving radium treatments with little or no experience, and in many instances with insufficient radium.

Hayward Pinch expresses the opinion held by all competent radiologists as follows:

"It is to be regretted that within the past twelve months statements have been published in the lay press to the effect that radium is a failure, and these appear to have originated in the pronouncements of some well-meaning but ill-informed practitioners concerning a sub-

ject of which they possess but very little personal experience. As these statements are not infrequently alluded to by patients and their friends, it is obvious that considerable harm has been done by their dissemination, and it therefore appears desirable strongly to controvert the assertion. Radium is not a failure when used intelligently and scientifically, and applied to the treatment of those conditions which experience has shown are amenable to its action. No honest worker claims, or has ever attempted to claim, that radium is to be regarded as a panacea, or as a cure for malignant disease, and many years must elapse and much more research and clinical work be done, before it will be justifiable to use the word 'cure' even in selected cases of malignant trouble. It is best, therefore, to speak only of 'arrest of the disease,' and this can be truthfully affirmed in very many instances. Patients whose lives would have speedily terminated, and who would have suffered much intense agony, have been enabled by radium treatment to live for many years in comparative comfort after all the known resources of medicine and surgery had been exhausted. That in radium we possess an addition to our armamentarium of great value, is a fact which cannot be challenged, and it is distressing to think that a rash and ill-advised statement, by its wide publicity, should have deprived many patients of fresh hope and possible benefit."

Levine has said, "Surgery, while meeting with some degree of success, has not solved the cancer problem. A comparative analysis of vital statistics and cancer statistics shows that in the hands of different surgeons, the highest percentage of all cancer cases of a community which can be cured by surgical treatment is 15.25 per cent, and the lowest 4.15 per cent, or, in all probability, less than 10 per cent."

*Read at the Seventh Annual Meeting of THE AMERICAN RADIUM SOCIETY, St. Louis, Mo., May 22-23, 1922.

Reprinted from the March, 1923 issue of THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, Vol. X, No. 3, pages 230-239. Copyright, 1923.

Radium, when properly applied, will bring about a definite inhibitory and destructive effect in the majority of rectal neoplasms. There is an abundance of evidence available to prove it to be a valuable adjunct when added to our present surgical procedures to combat rectal cancer, and that, in selected cases, it should be used as a pre-operative and postoperative measure.

The impossible is usually expected of radiation therapy. The majority of patients are beyond the aid of surgery or any recognized method of treatment. Many cannot be treated intensively. The majority of patients, three and five years ago, received inadequate and poorly applied treatment, when compared to our present methods. These factors make statistical study practically valueless.

The day is not far distant when cases will be classified as favorable or unfavorable for radiation therapy. The lesion may be grouped as one responding to radiation, but its location, extent and special characteristics will not permit of thorough treatment. The chief element of defeat is the lack of sufficient exposure of the tumor.

More than 300 cases in the Mayo Clinic have been treated. The majority were inoperable and only a reasonable amount of placebo treatment was given. Many of the treatments were postoperative and prophylactic. Some of the cases were recurring following radical surgical procedures. Twenty or more patients received pre-operative radium exposures. One or more, whose cases were operable, decided in favor of radium. In about 6 inoperable cases a radical posterior resection was performed after radiation therapy. No added surgical difficulties are recorded. A few patients stand out as receiving sufficient treatment to arrest the process.

McVay, in a study of 100 patients operated on in the Mayo Clinic for cancer of the rectum, made observations as follows:

"The anorectal lymph-glands are four to eight in number and are situated on the posterior and lateral walls of the rectum. The size of the growth in the rectum cannot be relied on as an accurate index to the probable lymphatic involvement.

Without lymphatic involvement there is a tendency of the growth to expand into the lumen of the bowel. The growths with some lymphatic involvement tend to spread by direct extension, and are slow growing. Carcinomas of the rectum, with extensive glandular involvement, tend to metastasize through the lymph stream early. Occasionally metastasis may take place by emboli breaking off into the portal vein. Rectal carcinoma is the most common form of intestinal growth, and represents 5 per cent of all cancers of the body. It is more common in men than in women.

"Metastatic involvement of the glands can only be definitely determined by systematic microscopic study of all the regional lymph-nodes. The size of the node is not an efficient means of determining whether or not there is metastatic involvement. This is particularly true if the amount of involvement is small or if the process is early."

Most cancers of the rectum are adenocarcinomas; the growth may be: (1) Bulky with partial or complete involvement of the walls of the rectum; (2) tabular with partial or complete involvement of the walls; (3) smooth, annular, and contracting with nearly complete obstruction; (4) multiple, occurring as polyposis. Each group presents difficulties for the radiologist. Each patient must receive individual treatment with applicators adapted to fit the requirements of intensive therapy. The cases can readily be classified into three groups:

1. *Operable Cases.* A digital, and in some instances, a proctoscopic examination, made the diagnosis. Exploration of the abdomen showed an operable growth in the rectum with no gross distant metastasis. A left rectus colostomy was made, and, a few days later, radical posterior resection was performed. As soon as surgical convalescence permitted, the deep end of the distal colostomy loop and the posterior resected area were treated with filtered radiation. Twenty-two patients received radium before resection; that is, two to three applications at intervals of two or three days. At the end of two weeks following the first application, the resection was

performed. One patient refused operation. Bare glass tubes were buried in the growth. A few other patients, on account of some contraindication to a general anesthetic or too great operative risk, received only radium treatments.

II. *Inoperable Cases.* The diagnosis was determined by either digital or proctoscopic examination, and in borderline cases, an exploration was made. A few operable cases, on exploration, revealed distant metastasis, or a second growth high in the rectosigmoidal area. The most outstanding subdivisions of this group are the few cases in which sufficient reduction of the tumor was obtained by radiation to warrant posterior resection. In some, a thorough microscopic search of the structures removed did not disclose cancerous tissue. I found 3 similar cases reported in the literature.

The first reported case of excision for cancer of the rectum following radium treatment was observed by Symonds in 1914. The patient, a man, aged seventy-three years, had an annular growth 4 cm. from the anus; on section it was found to be carcinoma. On five consecutive days, for six hours each, 100 mgm. of radium was applied, screened with 2 mm. lead and 3 mm. rubber. Eleven days later, visual and palpable examination revealed that the growth had disappeared and only a ring of cicatricial tissue was present. Six months and twenty-six days after the application of radium, a perineal resection was performed. The proximal end of the rectum was sutured to the anal portion and the sphincter was saved. Complete union followed. One month later, the colostomy was closed. Microscopic sections did not reveal the presence of active carcinoma.

The second case observed was reported by Handley. The patient, a man, aged sixty years, had a small bleeding area 12.5 cm. from the anus. Specimens removed for examination proved to be carcinomatous. The condition was considered inoperable. On September 6th, with the aid of a sigmoidoscope, 150 mgm. radium bromid, filtered through 2 mm. platinum was applied to the stricture above the ulcer area for nine hours. It was then applied

to a higher area for twelve hours, and to a lower area for ten hours.

Two weeks later, a severe local reaction occurred, but one month after treatment, the bleeding and pain had ceased. At this time, edges of the ulcer were flat, and the stricture appeared to be simple. Two months after the radium treatment, colostomy was performed, and the growth removed. At operation, 160 mgm. radium bromid filtered with 1 mm. silver, 2 mm. platinum, and 2 cm. gauze was applied in the abdominal wound for twenty hours, and 50 mgm. radium bromid filtered with 1 to 2 mm. silver, 1 mm. lead, and 4 mm. gauze in the perineal wound.

A large abscess in the right side of the pelvis had to be opened on the tenth day, and there was some suppuration in the abdominal and pelvic wounds. Sixteen days after operation, 150 mgm. radium filtered as previously was applied high in the pelvic sinus for twenty hours. One year later, the patient was in good health.

The third case reported was observed by Durand. The patient, a man, aged fifty-four years, had a circular neoplasm 2 cm. from the anus. The canal barely admitted the finger, and extirpation appeared difficult. One hundred and ten milligrams of radium was applied for forty-four hours. Five weeks later, a "Lisfranc operation" was performed. No added surgical difficulties are recorded. The lesion was found to be greatly modified and almost cicatrized.

III. *Recurring Cases.* The patients in this group had had radical resections, and some of them had had radium treatments postoperatively. They returned for further observation and treatment at varying intervals following operation. A few received marked palliative relief, and some were seemingly in good health. The relief from obstruction, the absence of bleeding, the lessening of pain, etc., account for the initial improvement. It is not easy to establish a diagnosis of recurrence. The character of the discharge may help; if possible, a small specimen should be removed for microscopic examination. In 1 or 2 patients in this group in whom recurrence was suspected, a hypodermic needle was introduced into the mass with

the escape of pus. With sufficient drainage, the condition cleared up.

TREATMENT

Cancers of the rectum are difficult to treat, since the tumor is incased in the bony pelvis with only a small contracted sinus in which to place the radium. If the inguinal glands are enlarged, they should be treated as metastatic processes. The radium is applied to the skin surface overlying the enlargement.

The treatment should be individual. I am confident that certain groups of patients cannot be treated according to a therapeutic framework. Every avenue of approach should be used in order thor-

oughly to radiate the tumor, and avoid accidental injury to adjacent normal tissue. The tumor tissue, if properly radiated, loses all morphology and is replaced by fibrous connective tissue. Overradiation should be avoided, especially in cases in which radical removal is under consideration in order to avoid added surgical difficulties. In selected cases, pre-operative radiation and a sufficient time interval before the radical removal will improve the case for surgery and give greater assurance against local recurrences. It will reduce to a minimum the chance of dissemination, since the primary growth has been almost completely devitalized, and has lost all power of rejuvenation. This has been

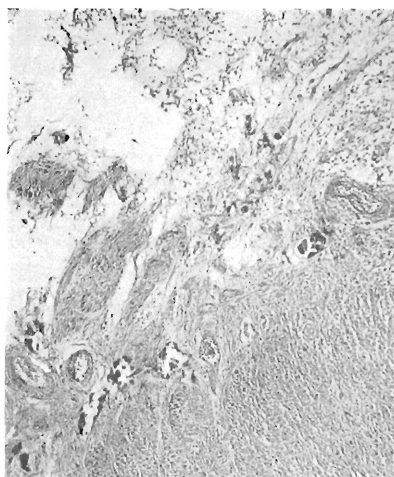


FIG. 1. Remains of carcinoma and musculature of rectum and apparent direct extension from primary carcinoma tissue completely devitalized.

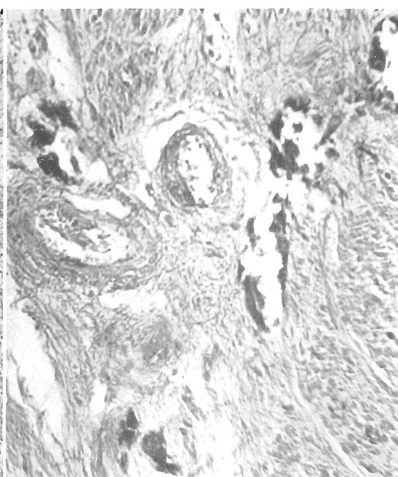


FIG. 2. High power of Figure 1.

oughly to radiate the tumor. The vaginal mucous membrane tolerates radium rays very well. If the rectal mass can be palpated by vaginal examination, the cavity should be packed with radium. The treatment should be either prophylactic or intensive, as the case demands.

Technique. The technique of radium application should be simple and yet consistent with good treatment. The applicator must remain as placed for the allotted time; this is assured by making the patient as comfortable as possible. The applicator should be designed so that it can be fixed to the body surface, to insure

proved by microscopic examination of specimens removed from the original tumor area (Figs. 1, 2 and 3). A minimal amount of exposure of doctor and nurse in preparing and placing the applicator should be an important factor in the construction of the applicators, and they have been adapted with these factors in view.

No distinction is made between the applicator containing a salt of radium, and a tube of radium emanation prepared by the Duane series of mercury pumps. Radium C, with its alpha, beta and gamma rays is the therapeutic principal, regardless of its source. The Universal tube applicator

with walls of silver 0.5 mm. thick, containing 50 mgm. radium sulphate by measurement, may be used, or a modified tube applicator (Fig. 4, No. 2) with walls of brass equal in filtration to the

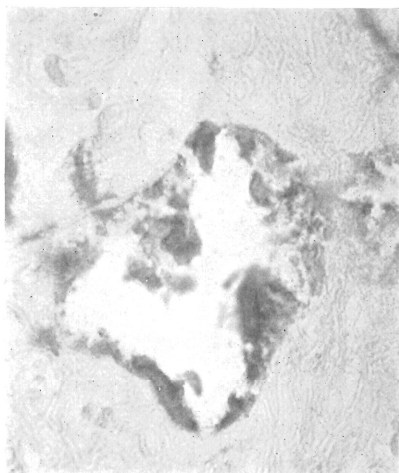


FIG. 3. Remnants of devitalized nuclei, impossible of regeneration.

silver tube, into which are placed small glass tubes containing emanation. The tubes usually measure 50 to 75 mc. The applicator shown in Figure 5, No. 2, is suited for the treatment of small and narrow sinuses, and can be introduced into drainage tubes at operation. The stem will bend to suit the contour of the body, and can be fixed with adhesive plaster.

To the stem (Fig. 5, No. 3) which has been devised to accommodate the Universal silver tube applicator, a brass shell is fixed with very thin walls, for it is not intended to act as a filter. A Para rubber tube, with walls 1.5 mm. thick, fits over the shell and extends 5 to 8 mm. beyond the end. This holds the radium tube in place and affords a soft rubber tip for the applicator, which will prevent undue trauma. It may be used similarly as the applicator shown in Figure 5, No. 2, but its extra bulk limits its application. It is the one of choice in treating a bulky tumor with a sinus of the rectum. With the index finger it can be easily directed through a tortuous canal common to bulky tumors.

The applicator (Fig. 5, No. 1) can be introduced easily. It is very efficient in the

treatment of the deep end of the distal colostomy loop; if used in this way, the brass filter is added (Fig. 4, No. 1). The wire stem permits easy introduction and secures fixation to the body surface.

The instrument shown in Figure 4, No. 6 is a modification of the soft rubber

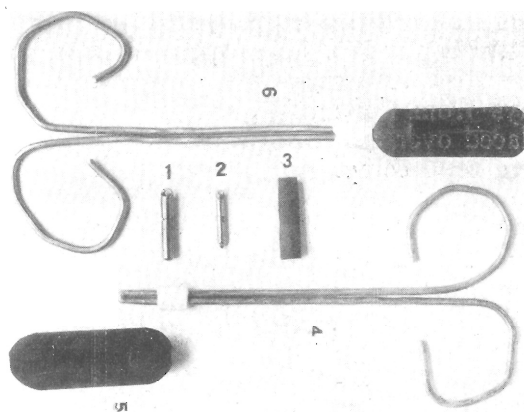


FIG. 4. No. 1. Universal silver filter with walls 0.5 mm. thick. No. 2. Modified Universal tube applicator; the walls are brass. No. 3. A rubber filter with wall 3 mm. thick. No. 4. A stem of solder wire 40 cm. long, with a small piece of adhesive tape around the tip to keep the stem from slipping through the canal in the rubber filter. No. 5. Part of a soft rubber Wales bougie (No. 10 or 12). The window accommodates one Universal tube applicator with or without the brass filter. No. 6. A modification of the soft rubber Wales bougie.

rectal Wales bougie. The unmodified bougie is very uncomfortable to wear for

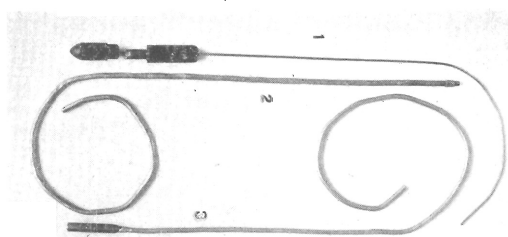


FIG. 5. No. 1. Wire stem and hard rubber tip with walls 2 mm. thick, into which the Universal tube applicator fits, with or without the extra brass filter. No. 2. A stem made of solder wire measuring 3.5 mm. in diameter and 40 cm. in length. The screw adapter at one end fits the applicator shown in Figure 4, No. 2. No. 3. A stem of solder wire. A brass shell is fixed at one end devised to fit the Universal tube applicator, and a Para rubber tube extends 5 to 8 mm. beyond the end of the tube.

any length of time. Some patients will not tolerate it at all. It does not permit accurate introduction, since the index

finger cannot be placed in the rectal canal at the same time.

The length of the part (Fig. 4, No. 5) may vary to suit the tumor, but if it is 6 cm. long, it is convenient, since it can be moved along the surface of the tumor. A strip of adhesive plaster is placed around the rubber part and then fixed to the stem; this makes a rigid applicator. The rubber filter (Fig. 4, No. 3) fits the window and is intended to absorb the soft secondary rays from the metal tubes. A finger cot placed over the end and fixed with adhesive tape completes the instrument. This

In the treatment of inguinal glandular enlargements, a wood block (balsa) 2.5 cm. thick and 3 by 4 cm. at the base is used to maintain the distance. Two millimeters of lead and 2 mm. of Para rubber are employed as filters. Fifty or 100 mgm. of radium in a Universal tube applicator is fixed to the block and allowed to remain twenty and ten hours respectively. The skin surface is mapped out in areas 3 by 4 cm. and from 3 to 6 areas are exposed in each inguinal region.

Radium can be buried in the tumor or ulcerated area. The standard metal needles



FIG. 6. A vaginal applicator which accommodates two Universal tubes. The brass wall is 1 mm. thick and is surrounded by 2 mm. of hard rubber. The outside diameter is 17 mm. and the length 4 cm.

applicator is very easily tolerated by the patient. It can be accurately placed with the index finger and securely fixed to the body surface. It is suitable in the treatment of small bulky growths and tabular growths which do not completely encircle the bowel.

The applicator shown in Figure 6 holds two Universal tubes. Friction holds the cap in place, and a finger cot covers the whole. Similar applicators have been in use for three years and have proved to be very satisfactory. Its chief use is in vaginal applications. It is placed with the patient in the knee-chest position and the distended vagina is packed with gauze; thus a minimum of normal tissues is radiated. It can be placed in a wide open wound of a posterior resection and held there with packing.

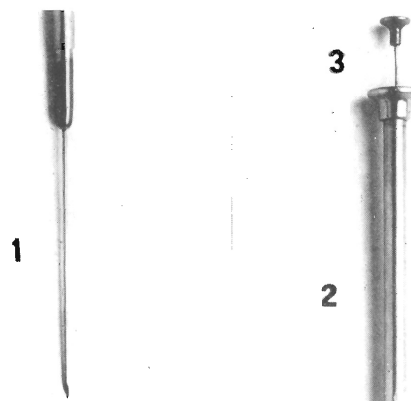


FIG. 7. No. 1. A spinal puncture needle, the end of which has been milled to fit the tube. No. 2. A brass tube made in various lengths, 20 to 40 cm. No. 3. A wire trocar long enough to dislodge the glass tube.

with walls 0.4 mm. thick, may be used, or bare glass tubes containing radium emanation taken from a Duane series of mercury pumps. An instrument is being perfected to facilitate the placing of the steel needles by direct and indirect methods. They may be placed by direct vision through a proctoscope or by the use of a brass cannula of sufficient size. The method of choice is by bare glass tubes.

Figure 7 shows the instrument employed in the bare glass tube technique; it consists of a needle (Fig. 7, No. 1), a brass tube (Fig. 7, No. 2) and a wire trocar (Fig. 7, No. 3) of sufficient length to dislodge the bare glass tube. If the needle and tube are made to be interchangeable, needles can be kept sharp, which is very important.

In burying the radium, general or local anesthesia is required. If the needles are

few in number and the mass small, the treatment is preceded thirty minutes by a hypodermic injection of $\frac{1}{300}$ gr. of scopolamin and $\frac{1}{6}$ gr. of morphin sulphate. Other anesthetic is not necessary. A general anesthetic is seldom used.

If our observations from treating the inoperable growths are correct, the operable growths should be exposed to radium, and after sufficient time has elapsed, probably six or eight weeks, the tumor area should be removed.



FIG. 8. (Case A100372). Specimen removed at operation.

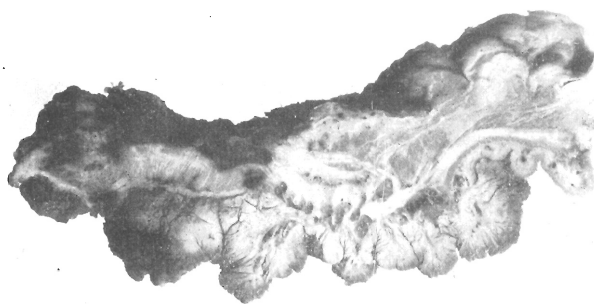


FIG. 9. (Case A100372). Longitudinal section of specimen shown in Figure 8.

"Surgical judgment" is not acquired in a few months, and may not be acquired for years; this is also true of radium therapy. The problems of the radium therapist are many. The patient, as well as the disease, must receive consideration. Should

Figures 8 to 11 show good examples of the lesions encountered in this group. The mass (Figs. 8 and 9) protruded into the lumen of the rectum, causing partial obstruction. It would be possible to bury radium needles in this bulky tumor.

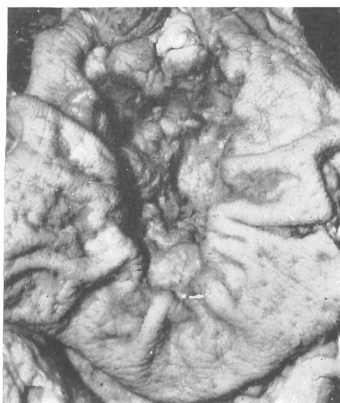


FIG. 10. (Case A170796). Specimen removed at operation; partial involvement of the walls of the rectum.

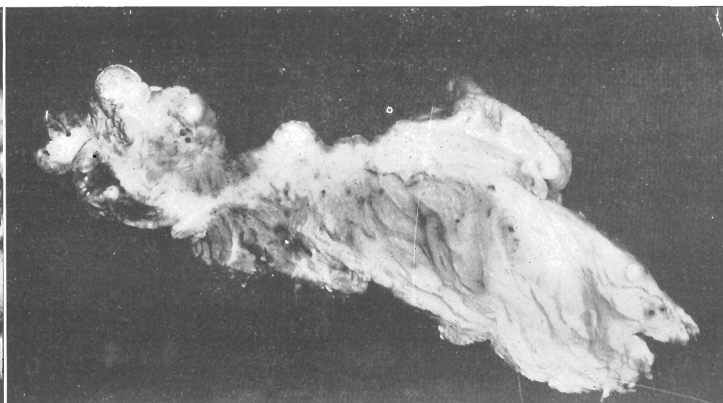


FIG. 11. (Case A170796). Cross-section of specimen shown in Figure 10.

the patient's health be greatly undermined on account of the disease or weakness following surgical procedure, the treatment is usually reduced in the number of applications. Each group furnishes its own problems.

The various types of tumors occurring in Group 1 require the widest range in technique. All buried radium treatment should be preceded by surface treatment. The extent is measured, and if it is within 4 to 7 cm., three treatments are outlined

and recorded as high, middle, and low positions. The applicator used may be the one in Figure 4, No. 6, or, in Figure 5, Nos. 2 or 3. Fifty milligrams radium is allowed to remain in each position for fourteen hours at one or two day intervals. If growths are small, brass filters should be used; otherwise, they are omitted. The majority of the 22 patients were operated on within ten and fourteen days after the first treatment. Definite gross changes in the tumor and edema in the tissues were noted, and the incidence of infection was suspected to be rather high. In order to manage the patients in this group more satisfactorily, more time (at least four to six weeks) should elapse, after the first treatment and before operation. This interval is essential in order that the treated area may heal and the tumor tissue be replaced by fibrous tissue. All over-radiation should be avoided. These cases require keen judgment and close cooperation between surgeon and radiologist.

If bare glass tubes are placed, the technique of Janeway is used. Tubes measuring 0.5 mc. are preferred. If the tumor is thoroughly radiated in this way, the results will be more certain.

In the inoperable group, Group II, the number of applicators is usually limited; the one of choice is that shown in Figure 5, No. 3. The canal through the tumor area is usually small and tortuous. The number of levels treated depends on the extent of the growth. Extensions in the region of the rectosigmoid area are the most tedious to expose, and these are usually undertreated. Three to four areas are the rule and are designated as high, middle, and low positions for application. Fifty milligrams is usually applied for fourteen hours in each area. A colostomy is not essential for this treatment, if, by abdominal exploration, the borderline case is found to be inoperable, and without obstruction. In some cases, the treatment will reduce activity and avoid impending obstruction. In this manner, the patient may get on without a distressing colostomy; however, an early colostomy is paramount in case obstruction develops. The most striking cases in this group are the ones made operable by radium treatments. Early metastasis is

not a characteristic of cancer of the rectum, and if reduction in the tumor occurs, posterior resection should be performed. The time interval should be six to eight weeks. All the patients in our series were thus treated. In cases reported in the literature, longer applications were made and more radium was applied. Our policy has been more conservative, and our local reactions are less. If the radium applicator can be placed in the center of a bulky growth, more radium and longer application are indicated. Overradiation should always be avoided, and possible surgical difficulties prevented.

Group 3, the recurring group, should continue to grow smaller. All patients operated on, and particularly those not previously treated, should receive post-operative radium and roentgen-ray therapy.

The applicator shown in Figure 5, No. 1, and the vaginal package (Fig. 6) are best suited to cases in Group 3. Brass filters are essential in the absence of the tumor, which is usually made use of to absorb the soft primary and secondary rays. Fifty or 100 mgm. tubes are used. The number of applications depends on the size of the cavity to be radiated. Three to five is the rule. The time is usually ten to fourteen hours. The vaginal package is fixed to a cord which aids in the removal, and is held in the Kraske wound with gauze packs. The interval between applications is two or three days.

All patients should be under observation. The treatments may be given at intervals of six and eight weeks, for the first six to eight months after operation. Every possible aid should be employed to establish a diagnosis of recurrence on account of a possible inflammatory process.

The primary growth in the rectum is but slightly affected by the roentgen ray. Even the newer apparatus, with voltages of 200,000 or more, gives disappointing results, and so we must look to radium for destruction of the primary lesion. On the other hand, metastatic nodules and lymphatic tissues are more susceptible to the roentgen ray.

The object of the roentgen-ray treatment is (1) to destroy or decrease in amount the lymphatic tissue and thus

decrease opportunity for metastasis, (2) to destroy or inhibit the growth of metastatic nodules.

The cases reported in this group were treated by the old technique, which consisted of a 23 cm. skin-target distance, filters of 3 or 4 mm. of aluminum, a spark-gap of 23 to 24 cm. between blunt points, and a current of 5 ma. sent through a broad focus standard Coolidge tube for five or six minutes. This formula produces a transient erythema in the skin, and at times causes slight pigmentation.

The rays were directed to the pelvis through 9 portals of entry, namely, 4 anterior, 4 posterior, and the perineum.

This method produced a somewhat effective cross-fire for the deep glands, and radiated the superficial glands, such as the inguinal and the perineal groups.

If these superficial lymphatic glands were definitely involved, they were treated with radium.

In the technique now employed, advantage is taken of the fact that a long skin-target distance assures nearly even distribution of radiant energy in the superficial tissues, and a large quantity of energy available for absorption in the deeper tissues. Nearly homogeneous radiation of short wavelengths is obtained by copper filtration and higher voltages.

The general reactions which usually follow the surface applications of radium and roentgen rays are similar to those seen in the treatment of other conditions.

They are, as a rule, a mild degree of anorexia, nausea, vomiting, and weakness. This lasts for twenty-four to forty-eight hours, and gradually disappears. The local reaction is tedious to evaluate. Some patients complain of an increase in mucous discharge, with or without blood, and very

little, if any, increase in pain. Urgency, frequency, and painful urination are seldom complained of. Proctitis rarely occurs. The technique, as described here, is very conservative, and severe local and general reactions are rare. In the buried technique, general and local reactions remain the same, although, on account of the impossibility of maintaining a sterile technique, infections occur. Ordinary cleanliness, enemas, irrigations, etc., are the only method, of preparing the field for the introduction of the needles. Fever of 102 to 104° F. has occurred, with the other usual signs and symptoms of general toxemia. Local peritonitis has occurred. The local complication may be hemorrhage and perineal abscesses. Mild hemorrhage is expected, and if severe, the rectum is packed with vaselin gauze through a proctoscope from the rectal side and if bleeding is from the distal colostomy loop, a long proctoscope, small in diameter, is placed in the loop and fair exposure is usually obtained. Vaseline packing may be introduced in a similar way as from below. The packing is removed in forty-eight to seventy-two hours. The patient is supported with the ordinary methods to control hemorrhage.

It is essential that accurate records should be kept. Figure 12 shows the possibility of a simple rubber stamp. It is self-explanatory.

SUMMARY

1. Radium, if properly applied, causes a definite inhibitory and destructive effect in the majority of neoplasms of the rectum.

2. Sufficient evidence is available to prove that radium is a valuable adjunct when added to our present surgical measures in the treatment of cancer of the rectum. The closest cooperation between surgeon and radiologist is essential.

3. In order to give the best possible individual treatment and to avoid discredit of either surgery alone or surgery and radium and roentgen-ray, an abdominal exploration should be made, except in gross inoperable cases.

4. Following exploration which determines inoperability with little or no low obstruction, it is not essential to make a colostomy in order to give the radium and

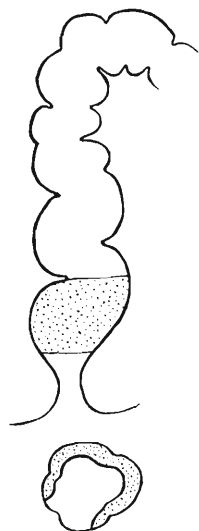


FIG. 12. A simple rubber stamp for the recording of accurate data. The dotted portion shows the extent of the involvement, height of lesion and rectal walls involved.

roentgen-ray treatment as outlined. Observation at intervals of from six to eight weeks is essential for the purpose of determining the advisability of radical operation.

5. The majority of patients with gross inoperable lesions should be given the benefit of radium and roentgen-ray therapy. A colostomy should be made at the first sign of impending obstruction.

6. The majority of patients receive inadequate treatment. It is impossible to give intensive treatment to some patients because of their general condition and because the entire tumor cannot be exposed. In patients with a colostomy, the growth should be treated through the distal loop. If the mass can be palpated by digital examination of the vagina, this cavity should be packed with radium in close proximity to the rectal tumor.

7. Early diagnosis is paramount. A digital examination should be made routinely of all patients. An early proctoscopic examination by an inexperienced physician is better than a late examination by a proficient proctologist. Microscopic examination is of definite value in early cases and will help to classify the cases, as well as to furnish a basis for prognosis when patients are operated on.

8. Some neoplasms of the rectum respond readily, while others are resistant to radium and roentgen rays. Long survival is possible in untreated cancer of the rectum.

Our conclusions must be guarded until a large series of cases is available and sufficient time has elapsed.

9. Since radium in larger quantities and high voltage roentgen-ray equipment are at present available, a combination of these is the most ideal method for radiation therapy, and results should be better.

BIBLIOGRAPHY

1. DA COSTA, J. C. Quoted by Cameron and Viol. *Radium*, 1921, xviii, 24.
2. PINCH, A. E. H. A Report of the Work Carried Out at the Radium Institute from January 1, 1921, to December 31, 1921. London, 1922, pp. 7 and 8.
3. LEVINE, I. The relative value of surgery, radium and roentgen rays in cancer therapy. *Urol. & Cutan. Rev.*, 1922, xxvi, 5-10.
4. MCVAY, J. R. Thesis—The Lymph Glandular Involvement in Carcinoma of the Rectum. May, 1920.
5. LABAT, GASTON L. Latest achievements of the art of local, regional and spinal anesthesia. *Ann. Surg.*, 1921, lxxiv, 673-683.
6. SCHOLL, ALBERT J., Jr. Sacral anesthesia in urology. *J. Urol.*, 1921, vi, 149-167.
7. SYMONDS, C. J. Cancer of rectum; excision after application of radium. *Proc. Roy. Soc. Med.*, 1913-1914, vii, Clin. Sect., 152.
8. DURAND, M. Cancer du rectum extirpé deux mois apres application du radium. *Lyon Chirurg.*, 1919, xvi, 408-409.
9. HANDLEY, W. S. Case of inoperable carcinoma of the rectum becoming operable under radium treatment. *Proc. Roy. Soc. Med.*, 1915, viii, Surg. Sect., 3-8.

Radium in the Treatment of Chronic Lymphatic Leukemia

Report of a Case in which Marked Remission
of Symptoms Occured under
Radium Treatment

FRANK E. SIMPSON, M.D.
CHICAGO

*Reprinted from The Radium Quarterly,
January, 1917*



Radium in the Treatment

of

Chronic Lymphatic Leukemia

Report of a Case in which Marked Remission of Symptoms Occurred under Radium Treatment

By Dr. Frank Edward Simpson
Chicago

For the privilege of reporting briefly the following case and for the history of the illness of the patient, together with the blood findings, I am greatly indebted to Dr. Chas. A. Elliott and Dr. Walter H. Nadler, under whose care the patient has been at various times in Wesley Hospital.

History.—P. D. C.—white—aged 38. The illness of this patient began in 1914 with swelling in the sub-maxillary regions following a “cold.” The swelling subsided but 6 months later it reappeared and tumors developed also in both axillae. From August 23d, 1916, to September 30th, 1916, the patient was in Wesley Hospital. Upon entrance to the hospital the white blood count was 300,000, and during his stay the lymphocytes ranged from 98% to 93%, the myelocytes from 3% to 3/10%, the polymorphonuclear leucocytes from 2.6% to 1%. The red blood count varied between 4,000,000 and 3,500,000. The hemoglobin averaged 70%.

During his stay in the hospital the treatment consisted of 12 X-ray applications at intervals of one week, two courses being given. At the same time Benzol treatment was administered. Under this treatment the white blood count was reduced from 300,000 to 71,400, and there was slight, but not marked reduction of the cervical and axillary tumors.

On January 12th, 1917, the patient again being

in Wesley Hospital, the white blood count was found to be 113,000. At this time (see Fig. 9), it was noted that the cervical glands were enormously enlarged, as well as the axillary, inguinal, and retroperitoneal, the latter being distinctly felt through the abdominal wall. The involved glands were painless, easily movable, and fairly soft to the touch. The spleen was found to be two hands breadth below the costal arch. At this time, January 12, 1917, radium treatments were begun and continued at intervals until January 30th. On account of various circumstances the application of the radium was carried out somewhat irregularly, but approximately 30 hours treatment was given over each area involved. The quantity of radium used was between 50 m. g. and 250 m. g. and the screening was the equivalent of 2 mm. of lead with 1 mm. of rubber. All other treatment was suspended.

On January 23, 1917, the white blood count was 73,000; on January 30, 1917, the white blood count was 14,000, and February 6, 1917, it was 5,400. The marked change in the appearance of the glands is shown in Fig. 10. This photograph was taken February 3, about three weeks after the beginning of the radium treatment. The remission of symptoms in this case was altogether satisfactory. A further report of the subsequent history of the patient will be given at some future time. 59 E. Madison St.

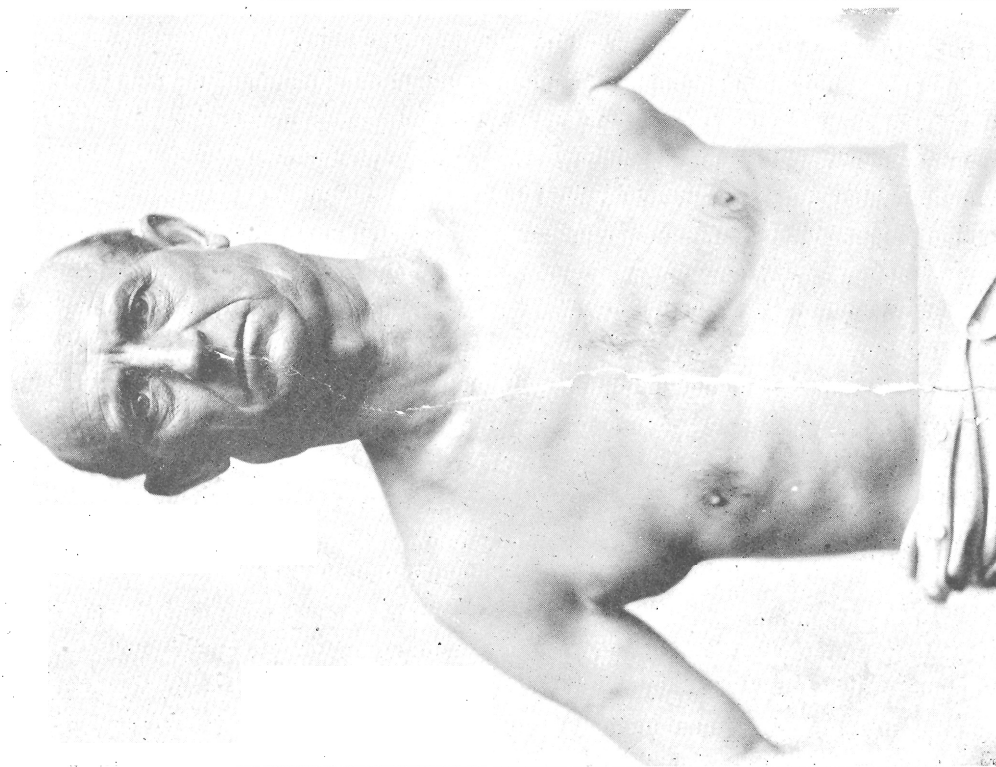


Fig. 9.—Chronic lymphatic leukemia. Note the enlarged cervical and axillary glands. Photograph taken January 12, 1917.



Fig. 10.—Patient in Fig. 9. Note the marked reduction of the axillary glands; the enlarged cervical glands have practically disappeared. Photograph taken February 3, 1917.

1999-2000
1998-99

2

THE TREATMENT OF PRIMARY CARCINOMA OF THE VAGINA WITH RADIUM

BY LEDA J. STACY, M.D.

Section on Medicine, Mayo Clinic
ROCHESTER, MINNESOTA

REPRINTED FROM VOL. IX, NO. I, JANUARY, 1922, PAGES 48-52

THE AMERICAN JOURNAL OF ROENTGENOLOGY

PUBLISHED MONTHLY BY PAUL B. HOEBER, NEW YORK

COPYRIGHT, 1922

THE TREATMENT OF PRIMARY CARCINOMA OF THE VAGINA WITH RADIUM*

BY LEDA J. STACY, M.D.

Section on Medicine, Mayo Clinic

ROCHESTER, MINNESOTA

I AM presenting this paper for the purpose of calling the attention of radiologists to the treatment by radium of primary carcinoma of the vagina, and with the hope of stimulating more frequent reports of such cases giving the methods of treatment and the ultimate results obtained. I have found only three cases reported in the American literature.

Ward, in 1908, reported a case in which the disease had extended, and a rectovaginal fistula had formed two months after the application of the radium. Levin and Griffith both reported cases in 1914; their reports were made three months after the completion of the treatment, and both local and general improvement was marked.

Primary carcinoma of the vagina is comparatively rare. Williams states that less than 1 per cent of all cancers in women are of vaginal origin. The lesion usually occurs between the ages of thirty and forty. Williams reported the case of the youngest patient on record, a girl of seventeen. He believes that the often quoted cases of Guersant and of Johannovsky in which the patients were three and one-half years and nine years respectively, were of sarcoma and not of carcinoma. In our series of 21 cases, the youngest patient was twenty-eight. Three patients (14.28 per cent) were under thirty-five, the average age was 50.14 years.

Apparently trauma is not an etiologic factor in these cases, otherwise carcinoma would occur more frequently, since the vagina is subjected to many injuries from childbirth, prolapsus uteri, and the wearing of pessaries. Seventy-six and nineteen hundredths per cent of our patients had had children. None of them had prolapsus of the uterus.

All observers report that the growth occurs most frequently in the upper

posterior portion of the vagina. In our series 42.8 per cent occurred on the posterior surface; 28.5 per cent on the anterior, and in 23.7 per cent there was involvement of most of the vaginal mucous membrane.

The course of the disease is very rapid. The average length of life following the first symptoms has been estimated sixteen and one-half months, the longest twenty-five to twenty-six months, and the shortest eight months. The rapid course and early glandular involvement are due to the free lymphatic supply of the vaginal mucous membrane.

Three groups of lymphatics drain into the pelvic glands from the vagina. A superior group arises from the upper third of the vagina and passes in front of the ureter, is joined by vessels from the cervix, and empties in the middle chain of the external iliac glands. The middle group comes from the middle third of the vagina and terminates in the hypogastric gland situated at the origin of the vaginal artery. The inferior group drains the lower third of the rectovaginal septum, travels along between the rectum and the sacro-recto-genital aponeurosis, and terminates in the gland of the promontory of the sacrum. The lymphatics of the vagina anastomose with those from the cervix, the vulva, and the rectum (Poirier, Cunéo and Delamere). This lymphatic supply explains the disappointing results in the surgical treatment of cancer in this location and also the subsequent glandular involvement when the local growth has been cured by radium. Metastasis to distant organs, however, is rare.

The symptoms of carcinoma of the vagina do not differ from those of carcinoma of the cervix. In our cases bloody discharge, leukorrhea, and in 52.63 per cent malodorous discharge, were noted. Pain

* Read at the Sixth Annual Meeting of THE AMERICAN RADIUM SOCIETY, Boston, June 6-7, 1921.

is not an early symptom and occurred in only 57.14 per cent. It is described usually as a low backache, or as inguinal.

Of the 21 patients with primary carcinoma of the vagina treated at the Mayo Clinic from July, 1915, to January, 1921, information concerning 14 has been obtained recently in answer to questionnaires. Seven of the 14 are living. One has lived three years and nine months, one two years and nine months, one two years and one month, one one year and two months, two six months, and one five months. Of those who died, one died two years and four months after treatment, one died one year and three months after treatment, one died one year after treatment, two died eleven months after treatment, and two died seven months after treatment.

SUMMARY OF CASE HISTORIES OF THE SEVEN LIVING PATIENTS

CASE I. Mrs. J. A., aged fifty-eight, had passed the menopause eight years before. For two years she had had a watery irritating vaginal discharge, recently tinged with blood, some pelvic discomfort and bearing-down pain. Examination showed a small papular roughness of the vaginal mucous membrane, slightly indurated and bleeding, on the left anterior wall of the vagina just within the introitus. No glands were palpable. Fifty mg. of radium salt were applied for six hours, directly against the ulcerated area. A specimen of the lesion removed one month later was reported to be inflammatory. The patient reported three years and nine months after treatment. She had recently lost 35 pounds in weight, but had no pelvic pain nor vaginal discharge.

CASE II. Mrs. H. G. F., aged eighty. Three months before the patient had noticed a growth in the posterior vulva, and occasional bleeding. A cauliflower growth, superficial, with very little induration, involved the posterior vaginal orifice and extended onto the perineum. The inguinal glands were not palpable. Two applications were made of the 25 mg. plaque for fourteen hours each, with 2 mm. brass and one-half inch gauze screening, and 2,000 mg. hours over the inguinal glands. Two months later 50 mg. radium

salt were given for ten hours and twenty hours respectively over the posterior vulva and perineum. The patient reported two years and nine months later. Her general health was good and there was no evidence of local trouble and no discharge.

CASE III. Mrs. J. J. B., aged fifty, menstruated irregularly, and had had pain in the back and hips, and occasionally intermenstrual bleeding for two or three months. She had lost slightly in weight. The posterior vaginal wall was indurated, nodular and with some ulceration extending to within half an inch of the introitus. The cervix was atrophied. No glands were palpated. Four vaginal treatments of 50 mg. hours of radium salt for fourteen hours, screening with one-half inch gauze and 2 mm. brass, and posteriorly by 2 mm. lead, and two rectal applications of 50 mg. hours for two hours, at intervals of from three to four days were given. X-ray exposures were made over the abdomen and back. The patient returned two months later. She had gained in weight and strength, and was free from pain and discharge. Examination showed two indurated and nodular areas, one in the posterior vault of the vagina and one just within the introitus. There was no evidence of glandular involvement. Two applications of radium to the vagina, two to the rectum, and x-ray treatment were given. The patient returned five months later still in good health and free from discharge. The vaginal mucous membrane was smooth, with slight induration in the anterior vaginal wall. The left inguinal gland measured 2 cm. by 1.5 cm. Another course of treatment was given as before, and also radium exposure over the inguinal glands. The patient was last seen in August, 1920. She complained of pain in the back and hips and down the right leg, and recently occasional slight amounts of dark blood passed by rectum; defecation was not painful. She had the same clear odorless vaginal discharge; she had not lost weight. The vaginal mucous membrane was smooth, the vagina slightly contracted. The left inguinal glands were enlarged and a few small glands were palpable by rectal examination. The rectal mucous

membrane was smooth. The patient was given one vaginal treatment of 700 mg. hours (50 mg. radium salt for fourteen hours), and 2,752 mg. hours over the left inguinal region. Two years and one month after the first examination the patient reported a poor general condition.

CASE IV. Mrs. W. M. S., aged sixty-two, had passed the menopause ten years before. For five months she had had a slight blood-streaked vaginal discharge, recently with a slight odor. She had lost but little in weight. An indurated nodular growth was found involving the vault of the vagina. Three cervical applications of 50 mg. radium salt for fourteen hours were given, one vaginal application of 68 mg. for ten hours and two rectal applications of 100 mg. hours each. Three months later three vaginal treatments of 700 mg. hours each and two rectal treatments of 200 mg. hours each were given. Six months later two vaginal treatments of 700 mg. hours each were given. The patient returned in six months, one year and two months after the first treatment, reporting a gain in weight and in strength, and practically no discharge. She was doing her own housework. The vaginal mucous membrane was found to be thickened and there was a small soft nodule on the posterior wall of the vagina. The vagina was shortened and the cervix flush with the vault. The left broad ligament was slightly thickened. A proctoscopic examination showed a slight ulcerated area on the anterior rectal wall. The patient was given x-ray treatment to the abdomen and back, but no more radium treatment.

CASE V. Mrs. C. E. R., aged thirty-six, had menstruated regularly. For four months she had noted an occasional bloody discharge and pain in the vagina radiating into the back. Her general health was good. An epithelioma 5 cm. in diameter was found on the posterior wall of the vagina. The cervix was free from involvement. No glands were palpable and the rectal examination was negative. The pathologist reported epithelioma, grade 3. Five exposures of 50 mg. radium salt for fourteen hours each, at from three to five day intervals, and x-ray

treatment over the abdomen and back were given. The patient returned six months later. She had gained in weight, had very slight, if any, vaginal discharge, and no pain. She had had two menstrual periods since treatment. The vaginal mucous membrane was smooth and not indurated; the cervix was free from involvement, and the uterus moveable. Examination of the rectum was negative. The patient was given x-ray treatments over the abdomen and back, but no further radium. She was advised to report in four months.

CASE VI. Mrs. A. F. C., aged sixty-nine, had passed the menopause twenty-two years before. For three months she had had a bloody vaginal discharge, and had lost slightly in weight. On the posterior wall of the vagina was a proliferating tumor about 2.5 cm. long. No glands were palpable. The pathologist reported epithelioma, grade 4. Three vaginal exposures of 50 mg. for fourteen hours, and x-ray over the abdomen and back were given. A physician who examined her recently found no evidence of malignancy and reported her general health good six months after the treatment.

CASE VII. Mrs. C. R. S., aged sixty-three, had passed the menopause seven years before. For six weeks she had noticed mucous vaginal discharge, but no bleeding. A proliferating growth 2 cm. to 3 cm. in diameter was found on the posterior wall of the vagina; it was superficial, and no glands were palpable. The pathologist reported squamous cell epithelioma, grade 3. The patient was given one application of 50 mg. radium salt for fourteen hours in a wax mould, and two days later emanation needles were buried to approximate 518 mc. hours. Four days later the growth was excised with a portion of the posterior vaginal wall. Twelve days later two more treatments of 50 mg. for fourteen hours were applied. The patient was recently examined five months after the first treatment, by a physician who reported the local and general condition to be good.

SUMMARY OF CASE HISTORIES OF THE SEVEN PATIENTS NOW DEAD

CASE VIII. Mrs. M. O., aged forty-three, had fallen astride a bathtub five

months before, and since then had bled irregularly and had noticed a swelling in the vagina. Examination revealed a cauliflower growth involving the anterior and the right vaginal wall. The uterus was movable. A total of 1,750 mg. hours radium into the vagina in three treatments, and two rectal treatments of 100 mg. hours each were given. The patient returned three months later stating that all discharge had ceased two weeks after the treatment, but a small new growth had appeared just within the vulva. Two vaginal treatments of 700 mg. hours each were given. When she reported one month later the vaginal mucous membrane was smooth and there were no adhesions. No induration was detected by rectal examination. Two months later there was found a small ulcerated area on the anterior vaginal wall and this was exposed to 600 mg. hours radium salt. The patient was not seen again until one year and three months after the first examination and eight months after the last radium treatment. There was no evidence of malignancy at this time and a diagnosis was made of a clinical cure. About six months later, however, she developed retroperitoneal tumors and died apparently of abdominal carcinoma, two years and four months after the first treatment.

CASE IX. Mrs. A. H. P., aged forty-one, had had a pus-like discharge for seven months, and soreness around the vulva at intervals. Examination showed an ulcerating growth posterior to the urethra, about 3 cm. in size. She was given 600 mg. hours over the growth, and returned in two months. At this time there was merely an area of induration at the site of the growth, and induration of the labia, but the inguinal glands on both sides were enlarged. She was again given two treatments of 500 mg. hours each and x-ray treatment over the glands. Three months later when she returned for examination there was rather a deep ulceration but it did not involve the urethra and the glands were still large and tender. Another series of 1,000 mg. hours radium salt was given as before, and x-ray treatment. The patient died one year and three months after the first treatment.

CASE X. Miss A. K., aged forty-four, gave a history of intermenstrual bleeding for from seven to eight months, and examination showed a carcinoma involving nearly all of the vaginal mucous membrane, associated with thickening in the broad ligaments. She was given three series of 20,000 and 21,000 and 22,000 mg. hours of radium salt respectively at three month intervals. There was local improvement but metastatic extension to the iliac glands, and the patient died one year after the first treatment.

CASE XI. Mrs. C. F., aged twenty-nine, had a large proliferating and ulcerating mass involving most of the posterior vaginal wall. This patient received 2,100 mg. hours by vagina (50 mg. for fourteen hours each for three applications) and 200 mg. hours by rectum. She improved after the first treatment, and three months later received a second series similar to the first. In two months, and again in three months she had severe hemorrhages, and died eleven months after the first treatment.

CASE XII. Mrs. R. McT., aged fifty-eight, gave a history of vaginal bleeding for one year. She had a polypoid mass 2.5 cm. long just within the orifice of the vagina, on the right and posterior surface, and nodules on both lateral walls; the inguinal glands were enlarged. She was given 1,200 mg. hours into the vagina. Improvement following treatment was only temporary and she died eleven months later.

CASE XIII. Miss M. Van O., aged twenty-eight, had had a watery discharge from the vagina for five months and pain in that region for three months. The entire lateral and posterior walls of the vagina were involved. The inguinal glands were not palpated. Three vaginal treatments of 700 mg. hours each and two rectal treatments 100 mg. hours each, were given. The patient returned three months later. She had had three hemorrhages two weeks before. The entire mucous membrane of the vagina was nodular and bled easily. An examination by rectum revealed marked thickening in both broad ligaments. Another series of treatments was given consisting of 728

mg. hours into the cervix, 300 mg. hours into the rectum and 1,400 mg. hours into the vagina. The patient died in three months, seven months after the first treatment.

CASE XIV. Mrs. E. L., aged thirty-two, had had a watery discharge of foul odor from the vagina for two months and pain for one month. Her menstrual periods had been regular. Examination revealed a large fungating growth on the left posterior surface of the vagina. The posterior lip of the cervix was granular, the inguinal glands were not palpated. Three vaginal treatments were given of 50 mg. radium salt for fourteen hours each and two rectal treatments of 50 mg. radium salt for two hours each. The patient died seven months later.

All the patients in this group were given x-ray treatments over the abdomen and back in conjunction with the local radium applications. As the technique of radium treatment improves the results will improve, particularly in the recent cases in which the emanation needles are buried in the growth, or in which much larger doses of radium salt are given. The increasing efficiency of the x-ray treatment is also an important factor. In our cases the local condition has been comparatively successfully controlled, but extension into the glands has not been prevented. We have no doubt been over-apprehensive of the development of vesicovaginal fistulas, and might have given heavier doses. Ves-

covaginal fistulas and rectovaginal fistulas occurred in one case, one year after the beginning of the application of radium, following the third series of treatments.

SUMMARY

1. Primary carcinoma of the vagina is comparatively rare.
2. The symptoms are similar to those of carcinoma of the cervix.
3. The disease extends early to the iliac glands; it rarely extends to other organs.
4. Radium and x-ray treatments offer better chances for a cure than surgery, and as the technique improves a larger number of permanent cures should be effected.
5. Better results are obtained and there is less danger of formation of fistula if the initial treatment by radium is heavy and not repeated, x-ray exposures to abdomen and back being, however, continued.

BIBLIOGRAPHY

1. GRIFFITH, W. S. A. Case of primary epithelioma of the vagina treated by radium. *Proc. Roy. Soc. Med.*, 1914, vii, Obst. and Gynec. Sect., 139-141.
2. GUERSANT. Quoted by Williams.
3. JOHANNOVSKY. Quoted by Williams.
4. LEVIN, I. Primary carcinoma of the vagina treated by radium and roentgen rays. *Med. Rec.*, 1914, lxxxvi, 195-197.
5. POIRIER, P., CUNEO, B. AND DELAMERE, G. The lymphatics. Chicago, 1904.
6. WARD, G. G. JR. Primary epithelioma of the vagina in a patient under twenty years of age. *Am. Obst.*, 1908, lvii, 723-726.
7. WILLIAMS, U. R. Vaginal cancer. *Med. Rec.*, 1901, ix, 841-845.

Radium

C. W. HANFORD, M. D.

CHICAGO

If 500 milligrams of radium were to be placed in contact with or in the center of a neoplasm for a period of fifteen hours, all cancer cells in a radius of an inch and a half would receive their death blow. But in accomplishing the execution of the lawless cells we would at the same time work havoc with perfectly healthy cells that happened in the path of the penetrating rays, causing serious necrosis in the immediate vicinity of the irradiation, besides general systemic disturbances of an unpleasant and dangerous character.

Therefore, we do not use 500 milligrams of radium element for a long uninterrupted session, but secure the ultimate death of lawless cells by dividing the total time of application so that if we should use this massive dose of radium, it would be in contact with any one point of the cancer mass but a fraction of an hour.

Kelly of Baltimore uses 500 milligrams of radium element in one applicator, applying the same to eight different points on the interior of the uterus in the treatment of myopathic hemorrhages. The applicator is left in each position but fifteen minutes, making the entire treatment one hour and forty-five minutes. This is all very well if we are fortunate in possessing 500 milligrams in one container. But the same end results can be obtained with 50 milligrams left in the uterus for twenty-four hours.

There are times when a massive dose of radium is much to be desired as, for instance, in irradiating growths in the mediastinum. In these cases one to two grams are employed, but are screened heavily with lead, besides being elevated several inches above the skin, that surface burns may be minimised. Burnham (*Jour. A. M. A.*, Sept. 20, 1917) reports several cases of mediastinal tumors that were caused to disappear under the influence of upwards of two grams of radium (2,000 milligrams).

The majority of us are working with less than one gram of radium and we cannot attempt such deep therapy with less than 500 milligrams.

As we lessen the amount of radium used we can increase the time of exposure. But in reducing the amount of radium we come to a point where the amount used would not destroy cancer cells, but on the other hand would act as a distinct stimulant to their growth. Prime of Columbia University in his experiments with chicken heart has found the lethal points of small pieces of tissue, where the unfiltered rays were concerned, was twenty, fifteen and ten minutes for 17, 83 and 100 milligrams of radium element, respectively. When the alpha and beta rays were removed by filtration with 0.4 millimeters of brass, three hours, one hour and forty-five minutes, respectively, were required for 17, 83 and 100 milligrams to kill; whereas when only the gamma rays and secondary beta rays were employed, twenty hours were necessary for 17 milligrams of radium and about seven hours for both the 83 and 100 milligrams to cause death.

The initial dose must be large enough to permit of a quantity of gamma or penetrating rays going through certain millimeters of tissue. And as these penetrating rays constitute but 1 per cent. of the total activity of radium, we have found by experiment and experience that there is a minimum amount of radium that can be used with certainty of cell destruction.

It was one time said that quantity of radium times period of application equals a constant. In other words, that one milligram of radium applied for 100 hours equals one hundred milligrams of radium applied for 1 hour. This is not borne out in practice, for the speaker has seen cases of malignant growths increase rapidly in size under the influence of sublethal doses.

It is true that the local ulceration of a carcinoma of the cervix will sometimes heal tem-

of radium applied for long periods. But such small doses have no influence on the cancer nests in the deeper structures of the organ. To reach these deeper nests it is necessary to employ at least 50 to 75 milligrams of radium for a total period of 60, 75 or even 100 hours. If large doses of radium are used it is not necessary to repeat the application each day until the total number of hours have been given. In fact, some patients do much better if a week is allowed to elapse between irradiations.

Radium has passed through many vicissitudes. It has been much maligned and highly praised and in both extremes seemingly satisfactory evidence has substantiated the derogatory criticisms as well as the laudatory claims. Therefore, it became evident that something was amiss, when two sets of observers, presumably honest and competent should note such widely divergent ultimate effects.

We believe that the reason for some of the adverse criticisms was due to the lack of knowledge of the physics of radium and consequently failure to apply it to insure beneficent results. But as time goes on we are learning that radium is a powerful agent and is not to be tampered with thoughtlessly and without care. We know that radium is productive of much harm improperly applied, but is of inestimable value when attention is given the rules governing the action of the rays on and through tissues.

The radium therapist early learns that all tissue is not affected similarly by radium.

There is a difference in the receptivity of cells to the rays. This receptivity varies with the age and race of the cell. Embryonal or undifferentiated cells are destroyed by the rays, while farther developed surrounding tissue undergoes only a simple or metabolic change. Some of the growths, such as lymphadenomata, pure sarcomata and fibromata are distinctly radio sensitive. But the growths peculiarly resistant to radium rays are the squamous celled epithelioma, fibrosarcomata and osteosarcomata. The adenocarcinomas are very amenable to radium.

In the early days of radium therapy, Schauta of Germany used from 50 to 100 milligrams of radium element in the uterus for periods ranging from three to eleven days. The results were disastrous. Of the 13 cases thus treated one died of pyonephrosis and eight showed fever, steady loss of weight, vomiting, tenesmus, diarrhea, headache and reduction in blood count. After

these drastic measures, the autopsies showed not a trace of carcinoma, but even so, the patients might as well have died from the disease as from the remedy. In this country we have all taken advantage of the mistakes made by the early investigators and are, thereby, securing the maximum lethal effect on malignant cells with minimum untoward action.

Schauta immediately realized his mistake and at once reduced the time of each exposure and increased the thickness of his screens. With this new technique he treated 11 cases of uterine carcinoma with exposures not to exceed 12 hours and would allow several days to elapse before the next application. He was very cautious while treating this series, this extreme caution being due to the unpleasant results following the treatment of the first series. In the manner above mentioned he gave from 5 to 8 exposures and after this would allow a rest of four weeks, when he would give a second series of shorter duration than the first. After a month a third series of still shorter exposures were given. Of these 11 cases 3 were somewhat improved and 8 remained apparently cured.

In carcinoma of the uterus the speaker has found that if the patients are well nourished with little or no cachexia, they can stand frequent exposures to 50 to 60 mgms. of radium and I often give four 15-hour exposures on consecutive days. This procedure is usually employed in inoperable carcinoma of the uterus. The patient is requested to return for a second series of irradiations. In cases of recurrence after hysterectomy, the same plan can be followed, though, as a rule, we do not give as many milligram hours in a recurrent case as in an inoperable or border line case. I have secured good results unaccompanied by nausea or fever by using 75 milligrams heavily screened and placed in the cuff in the vault and left for 24 hours. When left for this length of time, the next application should not be made till the lapse of three weeks. If the recurrence is localized, three of these exposures are usually sufficient.

When the patient returns after the first application or series of applications, all signs of ulceration have disappeared, as a rule, but it is not safe to allow this seeming healing, influence us to end our treatments, as there are no doubt active cells in the deeper tissues that require longer irradiations.

If the patient is in a weakened condition from

loss of blood or septic infection, a ten or twelve-hour irradiation is all they can bear. These exposures can be repeated every other day until four applications have been given.

The first effect of radiumization is cessation of bleeding and disappearance of odor. In some instances the pain associated with malignancy will be lessened or stop altogether.

The skepticism evidenced by some physicians, concerning the use of radium in malignancy, is due, I think, to the fact that they have not been permitted to observe the action of radium and again in some instances where they have witnessed its action, they have been unfortunate in viewing it through a veil of faulty technique. The dose has perhaps been too small or too large; too much or too little screening as well as insufficient or over-exposure.

Of course, the effect of over-exposure or insufficient screening is not so evident when radium is applied to the cervix or uterus as when used, for instance, in the rectum. In the latter situation it is never advisable to give an exposure of more than six hours when using 50 to 75 milligrams of radium. This dose can be repeated each day for three or possibly four days. In mucous membranes like the rectum, the screening should be such that only the penetrating rays pass. Otherwise contraction will result and in the rectum a marked proctitis will follow.

The bladder seems to withstand 50 to 75 milligrams for eighteen to twenty hours with very little evidence of irritation following. By using this dose if the applicator is placed directly in contact with the bladder neoplasm for a total exposure of 30 to 40 hours spread over several days, the mass will be greatly reduced in size after a month and all bleeding will have stopped. Even in cases where the bleeding has been quite profuse, it has ceased after the first application of radium. It will be necessary to repeat these irradiations at varying intervals, until the growth has disappeared. It is hardly necessary to say that not all of these neoplasms respond to radium, but it is rare to find one that is not influenced for the better and where pain, bleeding and irritation have existed, the patient experiences much relief after the irradiations.

It is quite simple to make the application of radium to the bladder if the growth is in the trigone, as it usually is, and especially so if a

through the urethra a 26 or 28 French urethroscope can be employed and the tube containing the radium with wire attachment can gently be pushed through and into the bladder, where it will lie in the confines of the trigone. If the neoplasm is on the lateral or anterior wall, special applicators must be employed. Barringer (*Boston Med. and Surg. Jour.*, Sept. 27, 1917) reports twenty-five cases of carcinoma of the bladder. Two of these he says would have been considered good operative risks. The other 23 were all impossible operative risks. In four of the twenty-five cases radium has locally removed the growth. One of these has been cystoscopically cured for 10½ months, one for five months and one recently. One has what is probably a slight local recurrence, although pathologic examination of a piece removed does not confirm this view. Barringer concludes the report by the statement that the results in these four cases shows that radium can do as much as surgery for cases of bladder carcinoma, without subjecting the patient to the danger and discomfort of a major operation.

Papillomas of the bladder are very amenable to the rays of radium and will disappear inside of two weeks. Of course, fulguration will destroy papillomas, but such destruction is not permanent, while the disappearance caused by radium is permanent.

Regardless of what others report, I have found carcinoma of the tongue and tonsil rebellious to radium. Perhaps one reason for this view is because I have seemed to get the case after everything else has been tried. The local evidence of cancer of the tongue or tonsil frequently disappears under the influence of large doses of radium. But there is such an intimate connection with the cervical lymph glands that metastases are present in the majority of cases. The cases I have seen in my individual work have mainly been those far advanced with great involvement of the surrounding lymph glands. By using large doses of radium a halt in the progress of the disease can be noted, but this is only temporary. I have had two cases of carcinoma of the tongue where the disease was localized, in which cases all evidence of the disease has disappeared under radium.

Leukoplakia and other superficial affections of the mouth and pharynx disappear quickly un-

go into the details of treatment of these cases, as the technique is quite simple.

It is well-known that sarcomas are readily destroyed by radium. I have treated three cases of sarcoma, occupying the pharynx and postnasal space, that have apparently disappeared. Last spring Dr. O. J. Stein reported to the Chicago Laryngological Society a case of sarcoma of the pharynx, post-nasal space and antrum which was cured by radium. He was positive the man was cured, as no sarcoma cells could be found at the autopsy. The patient died from an intercurrent disease.

Among the benign growths affected favorably by radium, fibroid disease of the uterus stands out prominently, as it is rare to find a case where radium does not reduce the size of the growth as well as exert a most beneficial action on the distressing symptoms, menorrhagia and metrorrhagia. To secure the best results, every effort should be made to introduce the radium tube into the cervical canal and uterus. The use of radium in the treatment of uterine fibroids is not new. In 1910 Wickham of Paris reported over sixty cases treated satisfactorily with radium. Abbe of New York treated his first cases of uterine fibroid 12 years ago and since then has treated 30 cases, always with pleasing results. He reports that he has yet to see a case which did not shrink, some completely, some rapidly, all in large measure. If the pressure symptoms are marked because of the size of the growth, it is the policy of most gynecologists to strongly advise operation. This procedure is adopted, not only because of the pain caused by the pressure, but because of the fear of malignant degeneration.

Another non-malignant condition of the pelvis readily cured in at least 99 per cent. of cases are the myopathic hemorrhages of the uterus. Clark of Philadelphia reports 100 per cent. of cures. The persistent hemorrhages that occur at the time of the menopause are permanently controlled by the use of from 40 to 50 milligrams of radium applied to the interior of the uterus for twenty-four hours. Occasionally it is necessary to repeat this treatment. Curettage should always precede this treatment, that the cause of the bleeding may be determined.

The last benign condition which I wish to speak about as applicable to radium therapy is

goiter. The size of the growth and the distressing symptoms associated with this disease are markedly lessened by the topical application of radium. Aikins of Toronto reports seven cases. In each case the growth eventually disappeared. The nervous symptoms subsided quickly and the rapid pulse came to normal. The action of radium is to produce a sclerosis, which is preceded by an obliterative endarteritis.

Just a word relating to radium and Hodgkin's disease: In selected cases of this disease, radium applied over the enlarged spleen will reduce the size of the latter and gradually bring about a lower white cell count. There are several reports of cases where all signs of the disease have disappeared. Ordway of Albany reports two cases of leukemia treated with radium where the white cell count was reduced from 500,000 to 6000, and the red cells increased from 2,000,000 to 5,000,000.

Before closing this paper I wish to speak briefly of radium as a prophylactic; its value for this purpose is recognized by all operators who have had even a limited experience with the power of the rays and to a greater degree by those who have given the subject more than passing notice. All operators have long known the limitations of the knife and though the most perfect technique is followed and the greatest care exercised in removing a malignant growth, the percentage of recurrences is large. Therefore they have turned to radium as the "hand-maiden" of surgery to pick up the wandering cells and prevent implantation.

From the opinions voiced by some of our leading operators, it would appear that we are rapidly approaching the time when the operator will not discharge his case after removal of a cancer mass, until the local area of the operation has been thoroughly rayed with radium. This should be done within two weeks after the operation. By observing this timeliness we are much more certain of controlling the recurrence and spread of the disease than if we wait until the return of ulceration. If the surgeon waits until the recurrence has actually taken place, there is the probability that the disease has extended beyond the area of ulceration and there is no certainty of reaching all points that have become infected.

Radium in Military Surgery.

BY WILLIAM H. CAMERON, M. D.,
Pittsburgh.

*REPRINTED FROM THE PENNSYLVANIA MEDICAL JOURNAL,
MARCH, 1916.*



and tissue destruction. In so far as I am aware, the utilization of the idea was first carried out by Dr. Joseph B. Bissell of New York, who secured splendid results in a small series of cases that had previously resisted all other surgical measures.

Being ambitious to develop a method that gave such promise, I was fortunate in securing the coöperation of several military surgeons attached to the R. A. M. C. who, like many of their fellows, were greatly concerned regarding the treatment of just such cases as I have mentioned. As a result of this interest, my associate, Dr. Benjamin R. Almquest, and myself were permitted to direct the clinical application of radium in several military hospitals in England. This work extended over a period of some ten months, and included observations on over one hundred cases.

Although the more important physical and chemical properties of radium have become a matter of general knowledge, it may be well at this point, to recall a few pertinent facts which have a direct bearing on the particular subject under discussion.

It will be remembered that radioactivity is a property of some forms of matter, and is due to a process of spontaneous atomic disintegration. Most forms of radioactive matter are characterized by the sending out of rays. In radium, these rays are of three types, the easily absorbed or alpha rays (which are positively charged helium atoms shot out with ter-

but having much greater penetrating power).

The measurement of radioactivity may be made in various ways as, for example, the observation of the effect of the rays on a covered photographic plate. Electrical methods of measurement are the simplest, and most readily give quantitative results. By means of the electroscope accurate measurements can be made of quantities of radium as small as one ten-thousand-millionth of a gram.

In radium we have, then, an agent that can be accurately measured, an important fact in scientific investigation. Moreover, it practically produces its effect without any appreciable disintegration (one half of any amount of radium element disintegrates in about 1700 years) and this property makes for therapeutic and financial economy.

In a communication of this character, it is impossible to give other than a general outline of the results obtained. It is also impossible to discuss in detail the relative value of this method over that of other methods universally employed by military surgeons. We desire to say, however, that we consider the bactericidal power of screened radium almost nil, and that its beneficial action resides in the power of the rays to penetrate tissue and, when used in proper amounts, to stimulate local circulation and cell activity. In other words, it is a convenient and more effective way of assisting nature than any other method devised.

While in England, I noticed accounts of a remarkable antiseptic solution developed by

Radium in Military Surgery.

BY WILLIAM H. CAMERON, M.D.,
Pittsburgh.

The suggestion that the stimulating effect of radium might prove of value in the treatment of such conditions as infected wounds, deep sinuses, nongranulating surfaces, etc., came after observing the effect of the rays when inadequate amounts were employed in attempted tissue destruction. In so far as I am aware, the utilization of the idea was first carried out by Dr. Joseph B. Bissell of New York, who secured splendid results in a small series of cases that had previously resisted all other surgical measures.

Being ambitious to develop a method that gave such promise, I was fortunate in securing the coöperation of several military surgeons attached to the R. A. M. C. who, like many of their fellows, were greatly concerned regarding the treatment of just such cases as I have mentioned. As a result of this interest, my associate, Dr. Benjamin R. Almquest, and myself were permitted to direct the clinical application of radium in several military hospitals in England. This work extended over a period of some ten months, and included observations on over one hundred cases.

Although the more important physical and chemical properties of radium have become a matter of general knowledge, it may be well at this point, to recall a few pertinent facts which have a direct bearing on the particular subject under discussion.

It will be remembered that radioactivity is a property of some forms of matter, and is due to a process of spontaneous atomic disintegration. Most forms of radioactive matter are characterized by the sending out of rays. In radium, these rays are of three types, the easily absorbed or alpha rays (which are positively charged helium atoms shot out with terrific velocity from the disintegrating atoms);

the more penetrating beta rays, which consist of negative electrons (particles 1700 times smaller in mass than the hydrogen atoms) moving with velocities approaching that of light; and the very penetrating gamma rays (a form of radiation analogous to the Roentgen rays, but having much greater penetrating power).

The measurement of radioactivity may be made in various ways as, for example, the observation of the effect of the rays on a covered photographic plate. Electrical methods of measurement are the simplest, and most readily give quantitative results. By means of the electroscope accurate measurements can be made of quantities of radium as small as one ten-thousand-millionth of a gram.

In radium we have, then, an agent that can be accurately measured, an important fact in scientific investigation. Moreover, it practically produces its effect without any appreciable disintegration (one half of any amount of radium element disintegrates in about 1700 years) and this property makes for therapeutic and financial economy.

In a communication of this character, it is impossible to give other than a general outline of the results obtained. It is also impossible to discuss in detail the relative value of this method over that of other methods universally employed by military surgeons. We desire to say, however, that we consider the bactericidal power of screened radium almost nil, and that its beneficial action resides in the power of the rays to penetrate tissue and, when used in proper amounts, to stimulate local circulation and cell activity. In other words, it is a convenient and more effective way of assisting nature than any other method devised.

While in England, I noticed accounts of a remarkable antiseptic solution developed by Dr. Alexis Carrel. It is not intended that

mm. Pulse running 108 to 110. Urine normal, chest normal. Diagnosis not positive. Injection of 100 micrograms radium element into median basilic vein to note effect on blood pressure. Some reduction in blood pressure but not marked. Concluded that high blood pressure was not circulatory.

19. L. P. Lacerated wound of back. Foreign body removed by operation. Sinus still discharging pus and nongranulating surface. Condition standing from June 22 to August 24. Improvement in discharge and better granulations after two applications.

20. P. McL. Lacerated wound of knee. Immediate operation for hemorrhage, wound infected. Some improvement noted in discharge after second application. Pain relieved. Pocket of serosinoid developed in old incision. Operated. Later had hemorrhage from wound and again operated. No applications after second operation.

21. J. I. Wound above right clavicle. Bone injured, small pieces of bone removed from time to time. Infected and considerable discharge from sinus. Standing for two months. Improvement noted in discharge from sinus after second application.

22. Wound of left shoulder. Bone removed by operation. Infected. Standing from May 15 to August 31. Pain and discharge much improved after first application.

23. S. A. Lacerated wound of leg; operated for foreign body. Condition standing from March 15 to September 2. Discharge improved, no pain, and reduction in swelling after first application of radium (35 milligrams used on this case).

24. J. L. Lacerated wound of leg, operated for foreign body; infection present. Sinus leading to bone. Condition standing from April 3 to September 8. Patient said there was no pain after first application of radium. Discharge cleared up after second application. Patient able to walk in ten days. Complete recovery.

25. P. P. Osteomyelitis of left upper femur. Standing since October 14. Bone removed by operation following August. Condition at time of radium application: Three openings leading to bone and discharging pus. In three days discharge less. In thirty days wounds entirely healed up. (Used cross-fire method on this case, 25-, 18- and 10-mgm. tubes being employed for ten minutes.

26. J. L. Lacerated wound over left iliac crest. Bone exposed, operated in July for foreign body. Condition standing from June 15 to September 15. Foreign body still in wound. Gave raying from 25-mgm. tube and on October 4, piece of shrapnel was removed by operation. Afterwards gave small dose and wound healed and closed up entirely.

27. L. C. Lacerated wound of elbow. Compound comminuted fracture. Operated for foreign body four days after injury was received. Operated for nerve four weeks after injury. Wound infected. Time of treatment, sinus presented discharging pus. Foreign body still present in wound. Condition

standing from April 24 to September 18. Five days after first raying, foreign body removed. After this, sinus was again rayed with a good result.

28. I. K. Lacerated wound of arm; compound comminuted fracture. Infected. Patient had temperature, local swelling and edema, discharge, etc. Concluded foreign body still in wound.

29. C. S. Compound comminuted fracture of arm, infected. Large open wound. Condition standing from August 15 to September 16. After first application, free from pain and wound in much better condition.

30. E. B. Penetrating wound of popliteal space. Foreign body removed and artery ligated by operation. Wound infected and considerable discharge. Condition standing from April 30 to September 24. After first application of 25-milligram tube, some improvement noted. May be that foreign body is in wound. Wound closed up on October 9.

31. W. T. Compound comminuted fracture of tibia. Infected. Sinus to bone. Condition standing from July 30 to September 27. After one application wound closed up in ten days.

32. R. P. Compound comminuted fracture of right tibia. Infected. Condition standing from June 20 to October 2, 1915. After first application and in about four days, healthy granulations over entire surface of wound.

33. C. R. Shrapnel wound of left temporal region. Bone exposed, soft tissue undermined. Not a favorable case for radium. No improvement after first application and no further treatment given.

34. P. D. Shrapnel wound upper part of tibia. Infected, bone removed September 24. Sinus leading to bone and discharging. Condition standing from July 3 to October 4. One application made and in ten days sinus closing.

35. R. W. Gunshot wound of arm. Sinus leading to fracture. Slight temperature, septic. Discharge of pus. Condition for about three months. In five days after first application, improvement was very marked.

36. L. G. Gunshot wound of left arm. Amputated and reamputated at upper third. Stump healed excepting discharging sinus. Condition standing from May 12 to October 18. After two applications, marked improvement in discharge and less pain.

37. C. L. Bullet wound through gluteal region; paralysis of bladder. Infected. Bullet removed May 18. Long sinus, obstinate discharge, considerable pain. Condition standing from March 23 to September 23. After several applications, character of discharge became less purulent. November 3, wound filling slowly and discharge much less.

38. Y. B. Shell injury to leg. Leg amputated and reamputated. Three discharging sinuses. Condition standing from June 15 to September 29. After three applications, decided improvement took place.

39. P. Y. Gunshot wound of shoulder. Two bullets removed. Sinus three inches long. Condition standing from April 22 to September 29. After sev-

applications wound is almost healed and no sepsis present.

V. T. D. Compound comminuted fracture of bones of arm. Nonunion. Waiting for sinus to close before operation. Condition standing from March 22 to October 13. No improvement after two applications. Treatment not continued.

U. S. Shell injury to shoulder. Foreign body removed. Discharging sinus to bone. After two applications, sinus closed and no discharge.

W. C. Gunshot wound left side. Foreign body removed and rib fractured. Discharging sinus. Condition of long standing. Considerable improvement in discharge after two applications.

X. A. L. Bullet wound left gluteal region. Bone removed by operation. Sinus extending to posterior opening to skin surface in front. Condition standing over five months. After three applications, sinus clean, less discharge and wound healing.

Y. M. Leg amputated May 18. Several recurrences. Sinus one to one half inches deep in condition standing from April 18 to October 1910. Two applications of radium, wound became clean and closing.

Z. W. Gunshot wound of hip. Sinus through bone. Condition standing from March 20 to October 2. Two applications of 25 milligrams of radium element; improvement very marked.

AA. G. Gunshot wound of arm. Bone and shell removed by operation. Condition standing over six months. Improvement after one applica-

O. Infected mastoid of long standing. General condition bad. Temperature 100° to 103° over long period of time. Pus dissected up tissues over large area of scalp and neck. Number of incisions made but patient would not permit radical operation. All other agents did not improve local general condition. Wound douched *t.i.d.* with 1% solution (2 micrograms to 60 c.c. aqua) moist dressing same solution applied. Given 100 micrograms four times a day by mouth. Three months following treatment, discharge was reduced. Ten days infection cleared up. Temperature normal and patient able to be up.

CONCLUSIONS.

The application of a stimulating dose of radium rays (ten to thirty-five milligrams of

element, in tubes, from ten to twenty minutes) is the most effective agent employed up to the present time in the treatment of wounds in what may be called the subacute or chronic stage of infection. The same may also be said of nongranulating wounds.

2. By raying to the point of tissue destruction, the removal of sloughing tissue, dead bone, etc., may be facilitated.

3. In raying deep sinus cases, care must be taken to place tube at bottom of sinus. If foreign body prevents, the case should not be rayed until same has been removed, unless the raying is intended to facilitate the removal of bone spicula.

4. The number of cases already reported will demonstrate that the intravenous injection of radium is void of danger. Its effect on the circulation, the clotting period of the blood, on the red and white cells, and its effect in increasing the action of other agents makes it a most valuable agent in the treatment of shock, anemia, and cases presenting symptoms of general infection.

5. Although the opportunity for using a solution containing radium element has not been very large, in the treatment of acute infected wounds, enough data has been collected to demonstrate that its use in combination with normal saline, will give just enough stimulation to local circulation to bring the white cells constantly into action.

6. Radium rays have no bactericidal action and the effect, when used locally, is due to the stimulating effect of the rays.

7. Because of the long period of time radium tubes may be employed, and the number of cases capable of being treated in twenty-four hours, we believe we have developed the most economical method of treatment of backward wounds.



Roentgen Therapy in Chronic Sinusitis

F. E. BUTLER, M.D. AND IVAN M. WOOLLEY, M.D.

PORTLAND, OREGON

Reprinted from
The Western Journal of Surgery, Obstetrics and Gynecology
July, 1932

RAJENDR
VIRAJ

Roentgen Therapy in Chronic Sinusitis*

F. E. BUTLER, M.D. AND IVAN M. WOOLLEY, M.D.

PORTLAND, OREGON

OUR desire to observe the effect of roentgen therapy on chronic sinus infections dates back to the early days of injection of the antra by opaque substances, together with the early pathological reports showing hyperplasia of lymphoid tissue in the removed membranes.

constant drainage and of marked constitutional symptoms during the exacerbations. Radiographs following lipiodol injection showed a membrane ranging from four to eight mm. in thickness in the right antrum.

The patient consented to roentgen therapy rather as a last resort before surgery, and was given a full erythema dose over the affected antrum,

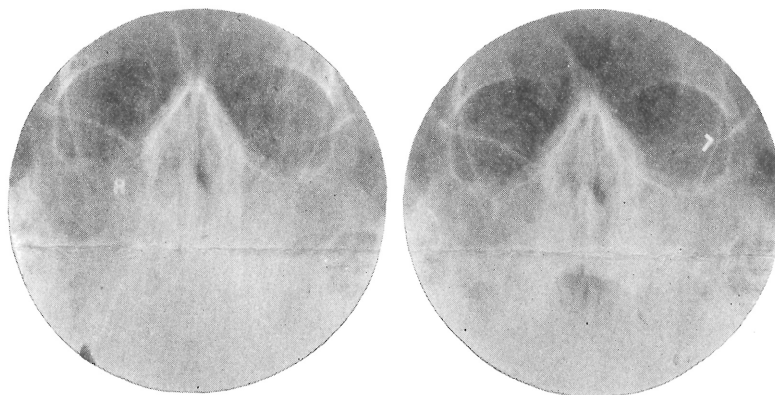


Fig. 1. Typical illustration of that type of case where no radiographic evidence of improvement can be seen, even after a repeated treatment. This patient, however, received a complete clinical relief from secondary manifestations that were considered to have been due to antrum infection.

The first opportunity presented itself in April, 1930.

CASE REPORT

One of our technicians reported that she had been advised by her rhinologist to have a radical antrotomy. She had been under treatment by a competent physician for over ten months, and during this time had had repeated sinus washings. Her upper teeth had been extracted and socket drainage established. She complained of almost

using 120 K. V. P. 5 M.A. 10 inch distance and 3 mm. aluminum filter. During the following 24 hours there was a profuse, bloodtinged discharge from the nose and through the fistula in the mouth, and the patient complained of a moderate headache. Her temperature was 100.5. The following morning, however, she reported for work feeling well; and from that time has had no further trouble with the right antrum.

Radiographs taken four months after the treatment showed a marked shrinking of the previously thickened membrane.

Six months following the treatment the patient contracted a severe cold, which produced an acute sinusitis of the left antrum. The right antrum,

*Read before the 19th Annual Meeting of the Alumni Association U. O. Medical School, Portland, Oregon, March 7, 1932.

which had been treated, gave no trouble. Radiographs at that time showed a marked haziness of the left side, while the right antrum appeared clear. The left antrum was then irradiated and promptly cleared up, without the reaction experienced following the former treatment. This girl is still in our employ and has had no further trouble with the sinuses (over two years).

This encouraging result stimulated further work, and the literature was searched for additional information.

referring physician, and the cases here reported were checked radiographically and clinically.

The results obtained at this time are as follows:

Thirty-one cases were cleared up clinically within five to six weeks after treatment. Fifty cases were improved but not completely cleared up. Nineteen cases were not improved. All the patients had more or less nasal discharge.

Twelve complained of neuritis, in

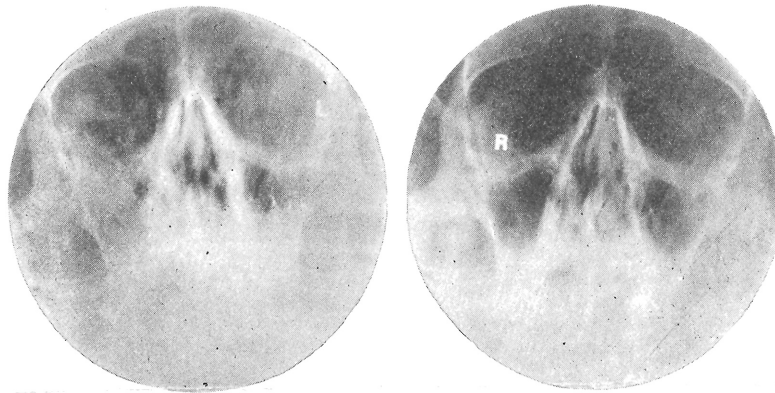


Fig. 2. Woman, age 28, under treatment for six months prior to Roentgen therapy. Demonstrating the result obtained by one Roentgen treatment.

The only article found in the American literature was one by Dr. John D. Osmond, of Cleveland, which was read before the Radiological Society of North America at Los Angeles in 1922, and was published in the American Journal of Roentgen and Radium Therapy of May, 1923. However, this article dealt with acute cases only. Our search for roentgen treatment in chronic cases failed to reveal any data on that subject.

At the time this paper is being written, over one hundred patients suffering from chronic sinusitis have been treated by the authors.

These cases were not selected by us, but were referred to us by physicians after the usual therapy had failed to give satisfactory results. During the time these patients were under treatment they remained under the observation of the

which the sinuses were considered the focus of infection. Of these, nine were completely relieved, one improved and two could see no improvement.

Four complained of constant headache, which subsided following treatment. Five suffered from chronic bronchitis and these were all relieved.

As these cases were studied it was observed that those having the most marked symptoms showed the greatest improvement. The largest percentage of those not improved were patients whose sole complaint was a chronic nasal discharge.

This variation of response may be explained on the basis of microscopic examination of the excised tissue from chronically infected sinuses. Three major types of tissue structure are found in such studies: the hyperplastic, the atrophic, and the mixed hypertrophic and atrophic.

The first or hypertrophic group are classified into two sub-groups, depending upon the amount of lymphoid tissue included.

The excised tissue in the first sub-group is made up of a preponderance of lymphoid cells in comparison with the fibrous material. Patients in this sub-group usually produce a radiograph showing a markedly thickened membrane with or without polypi, lining the antral wall with a fairly clear center cavity, and it is in this group that the best results are obtained by roentgen therapy.

CASE REPORT

One of our patients of this type was a girl twelve years of age who had been under almost

a window operation into the antrum, was irradiated. Three weeks later he sloughed out a large polyp and his symptoms promptly subsided.

The members of this hyperplastic group have been the ones in our series to experience the greatest reactions. There is usually an increased discharge for several days, the discharge in some cases being blood tinged. These sinuses are usually clear of pus in from three to six weeks, and radiographs taken at that time show an antrum which appears normal, the membrane usually having subsided to normal.

It is in these cases that the careful co-operation of a competent rhinologist is indispensable. Should the ostia of the cells become occluded and free drainage there-

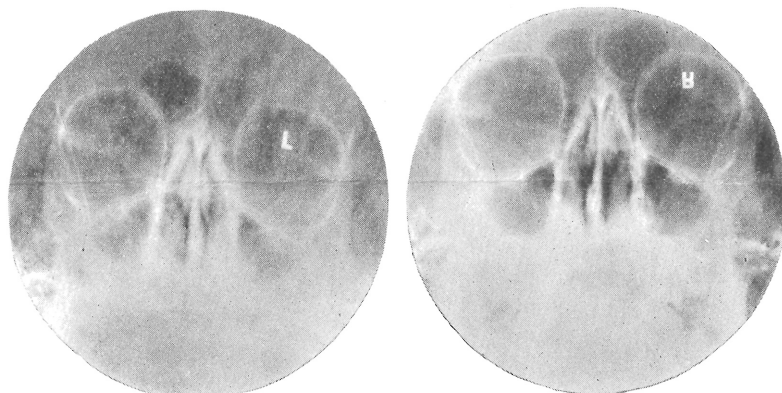


Fig. 3 (see second case report). Child, age 12, demonstrating the result of one Roentgen treatment.

constant treatment for four years. She spent as much time as possible at the seashore, where she was more comfortable, but was never free from distress.

At the time she was referred for roentgen therapy, the radiographs showed a large polyp in the left antrum, with a marked thickening of the membrane in the right. She was given one treatment and experienced a marked reaction for several days. Since that time she has been entirely free from her previous symptoms, and a radiograph taken recently shows both antra clear, with a complete disappearance of the polyp, despite the fact that she was just recovering from a cold.

Another patient referred by the same physician, following several months' treatment, including

by interfered with, the patient will suffer the discomforts of acute suppurative sinusitis, and unless drainage is reestablished, marked constitutional reactions may develop, even to the possibility of septicemia. It is for these reasons that we instruct our patients to remain under the observation of the referring physician until he feels that they have progressed sufficiently to be discharged.

In those cases in which hypertrophy is due to a preponderance of fibrous tissue the results are quite different. Following irradiation, the general reaction is less, the discharge only slightly increased, if at all, and persists for a longer period of

time. Radiographic examination following treatment often shows an increase in the density of the membrane rather than a shrinking. These cases as a rule have shown much slower improvement and

in which the antra alone were treated without satisfactory results, subsequent irradiation of the ethmoids produced prompt relief.

Our experience with the atrophic type

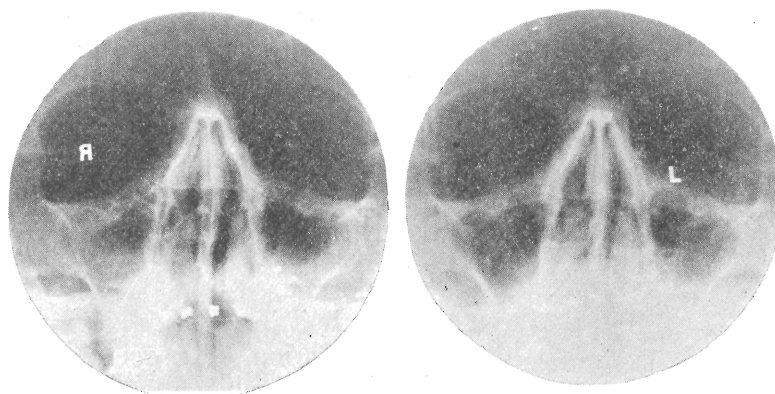


Fig. 4. Patient under treatment for three years prior to Roentgen therapy. Demonstrating the result obtained in one Roentgen treatment. This patient developed a severe coryza one year later, which cleared up in a few days without special treatment. Radiographs taken at that time showed the antra to be normal.

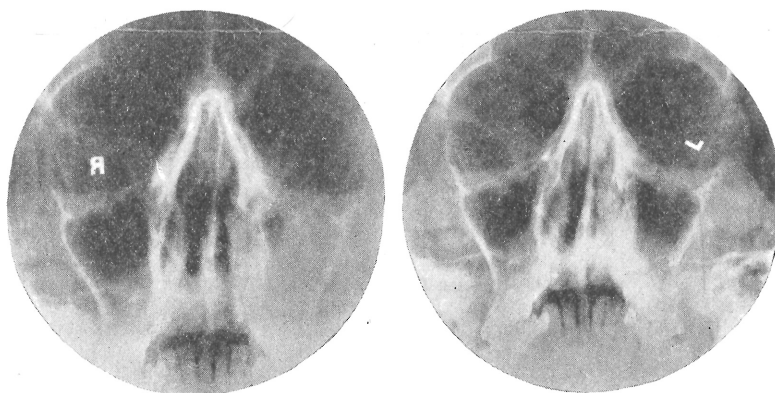


Fig. 5. Left antrum treated for three months before submitting to Roentgen therapy. Demonstrating the result obtained in one Roentgen treatment.

usually require more than one treatment. The discharge has continued for some time, but the patients have shown improvement and often complete relief from symptoms resulting from sinus infections.

The results obtained from treatment of the ethmoids are more difficult to check than are those of the antra, and we have to rely principally upon the symptomatic reports. However, in several of our cases

is somewhat limited. We previously refused to undertake roentgen therapy in these cases. Recently, however, a patient of this type was referred because he had failed to respond to all other therapy. He was given a lighter dose than was used in our other types and has been relieved for four months.

Since that time we have treated several of these patients, using small frequent doses with some good results. These cases

have been too few and the time too short to draw any conclusions concerning them, but we believe many will improve under small stimulative doses.

Acute cases are not included in this report, although we have had excellent results using lighter doses than those given for chronic conditions.

The technic used in this series has been as follows: 120KV. P. 5 M. A. ~~10~~ ^{eleven inch distance} inch distance, 4 mm. aluminum filter. Each sinus was irradiated separately for ten minutes. Over the antra a port one and one-quarter inches in diameter was used, and for the ethmoid and frontal areas the port was varied by means of lead foil to conform to the proper areas. The dosage thus given is 800 ~~roentgen~~ ^{roentgen} units as measured by a Victoreen instrument. The eyes were shielded at all times. The rays were directed in such fashion as to produce a cross firing of the posterior cells when all the sinuses were treated.

The factors above mentioned, when used on our therapy apparatus, produced a mild erythema over the antra in about one-third of the cases treated, but we have observed no reactions following treatment over the ethmoid or frontal regions because of the smaller port used.

In closing, we wish to state that this report is being given at this time in order to stimulate interest in this field of therapy; that we may learn of the experience of those who may have pursued similar work, and to encourage others to investigate this problem, so that accurate information may be obtained as to the

efficacy of this type of treatment.

We wish to make it clear that we do not consider that this report conclusively proves roentgen therapy to be a definite cure for chronic sinusitis, as the number of patients treated has been small and the elapsed time not great enough accurately to evaluate the results.

We do feel, however, that roentgen therapy, properly used in cooperation with a competent rhinologist, will greatly aid the recovery of better than fifty per cent of these cases.

CONCLUSIONS

1. One hundred cases of chronic sinusitis treated by roentgen therapy are here reported. The majority of these cases were referred for treatment by competent rhinologists following unsuccessful medical and surgical therapy and for the most part were those in which radical surgery was being considered as the only means of securing relief.

2. These patients have been under observation for varying lengths of time during the past 18 months.

3. The results obtained thus far are, 30 per cent cured, 50 per cent improved, 20 per cent unimproved.

4. It is essential that this type of therapy should be conducted with the close cooperation of complete clinicians.

5. The authors consider this to be merely a preliminary report, as the elapsed time and number of cases are too small for accurate interpretations.

Small, dark, irregular marks or smudges.

01

8

Small, dark, irregular marks or smudges.

1

RADIUM TREATMENT OF TOXIC GOITER WITH METABOLIC DEDUCTIONS

BY R. E. LOUCKS, M.D., C.M.

DETROIT, MICHIGAN

REPRINTED FROM VOL. X, NO. 10, OCTOBER, 1923, PAGES 767-776

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

PUBLISHED MONTHLY BY PAUL B. HOEBER, NEW YORK

COPYRIGHT, 1923

RADIUM TREATMENT OF TOXIC GOITER WITH METABOLIC DEDUCTIONS*

BY R. E. LOUCKS, M.D., C.M.

DETROIT, MICHIGAN

IN order that the true significance of a pathological condition or dysfunction of the thyroid gland may be understood, it is absolutely necessary that the anatomic relation with physiologic function and normal metabolism should be known, with a comprehensive understanding of its relation to the other endocrine glands.

Anatomically the gland consists of two lobes connected across the second and third ring of the trachea by an isthmus. The posterior surface is in contact with the thyroid and cricoid cartilages, the inferior laryngeal nerve, the inferior constrictor of the pharynx and the lateral borders of the trachea and esophagus. The outer surface is covered with the superficial muscles of the neck and the external jugular vein. The outer border of each lateral lobe is in close proximity to the carotid sheath containing the common carotid artery, the internal jugular vein and the pneumogastric nerve. The significance of this relation is apparent when dealing with any one of the enlargements of the gland.

The physiological function appears to control the iodine and calcium balance and split up iodine products into thyroxine (Kendall) which acts as a hormone stabilizer to the whole endocrine chain. The one or the many hormones have specific function in cerebration of the brain cells, increasing the activity of nerve transmission and regulating the heat mech-

anism; in fact, they are the main activators of metabolism.

Normal metabolism signifies a harmony in all the functions of the living body that go to make up a "well being." A physiological activation is not by any means a pathological hyperactivity.

The question arises: When is a hyperactive thyroid a pathological disease? The answer: When symptoms of toxicity are manifest, either objectively, subjectively, or by laboratory calculations.

Suffice to note that a toxic goiter may be:

1. A primary exophthalmic,
2. A toxic adenoma,
3. A toxic adenoma with exophthalmos.

1. The objective symptoms are manifest in the exophthalmic type by (a) the prominence of the eyeballs, giving a staring expression and a facies of mental alertness, (b) a lagging of the upper lid in looking down so that it apparently covers more than its half of the eyeball when closed. At times the lids cannot cover the ball completely but leave a slit allowing the conjunctiva and cornea to become injected from exposure, lack of palpebral lachrymation and massage. A strip of white sclera shows between the cornea and lower lid when the eye is open. (c) There may also be winking, tardiness of external ocular muscles and decreased lacrymation. (d) At times a red tremulous tongue is found and also teeth notched on the lateral borders.

* Presidential Address read at the Annual Meeting of THE AMERICAN RADIUM SOCIETY, San Francisco, Calif., June 25-26, 1923.

The primary exophthalmic type may not show any noticeable change either in size or figure of the gland, while the adenomatous type presents variations in size, from the large prominent uneven mass to small lobulated cystic out-croppings on the lobes or isthmus.

Pulsations of the thyroid arteries are common and a bruit may at times be heard over either lobe. The radial pulse varies from 90 to 160 and often registers much less than the apex beat, as each wave does not have time to be carried independently.

The heart may be enlarged in all diameters and if the case is of long standing there is evidence of myocardial degeneration, as elicited by the degree of fibrillation and the character of the murmurs present. The precordial impact may be diffuse, and have enough force to cause a heaving of the chest wall with each contraction of the heart. Pulsation of the superficial arteries of the fingers and toes is common.

The systolic blood-pressure in primary exophthalmic cases is at first raised, but gradually returns to normal or goes below normal after the first crisis. Should spontaneous cure succeed, it remains low; but should a second crisis occur it again rises and remains high until the termination of life, unless treatment controls the toxicity. The diastolic blood-pressure is usually low, giving a much increased pulse pressure.

Trophic symptoms occur as a brownish yellow pigmentation of the skin, thinning of the hair and longitudinal striae of the nails.

Mental disturbances are common in the late or very active cases and vary from a state of constant fear and apprehension to that of a decided psychosis.

2. Subjectively, the individual complains of nervousness, general weakness, palpitation, insomnia, pulsation in the ears when lying down, sweating of the hands and feet and, at times, general hyperidrosis. Frequently digestive disturbances occur, such as nausea, loss of appetite and diarrhea; menstrual irregularities in females; pain and pressure in the neck with a sensation of choking, or an irritable cough, and general feeling of "fag."

3. Laboratory calculations are most conclusive in the toxic state. Du Bois has standardized basal metabolism in the normal individual and Plummer has proven by extensive studies that thyroxin in excess raises the metabolic rate. Therefore, a sufficiently high metabolism is pathognomonic of thyroid hyperactivity and is one of its most important diagnostic features.

With hyperactivity of the thyroid, there is marked increase in cellular activity and carbon dioxide output, with a speedy demand for larger oxygen consumption. To determine the metabolic rate it is necessary only to measure the amount of oxygen consumed for a given period of time, and make calculations in calories per hour, by comparing the intake to certain physiological standards for body surface, temperature and barometric pressure.

Urinalysis reveals kidney changes in direct relation to cardiovascular degeneration and digestive disturbance. Scanty, high-colored urine signifies concentration due to evaporation and skin elimination. Albumen and casts are indicative of kidney dysfunction and contraction. The presence of sugar indicates diminished carbohydrate toleration.

The blood picture may reveal a decreased number of erythrocytes with lessened hemoglobin content or an increase in leucocytes with a larger percentage of lymphocytes and eosinophiles.

Blood chemistry shows an increase in blood sugar only, which is provided by the thyroid for an increased heat production. If the blood sugar rises slowly there is a compensatory function of the kidney that holds the balance, and there is no glycosuria. Should this tolerance be broken by increased carbohydrate ingestion, the kidney excretes sugar.

An editorial in *The Journal of the American Medical Association* for April 14, 1923 (page 1071) after discussing the roentgen rays and surgery in the treatment of exophthalmic goiter, says: "In the light of the present-day evidence, the choice of therapeutic procedure presents, indeed, a difficult perplexity."

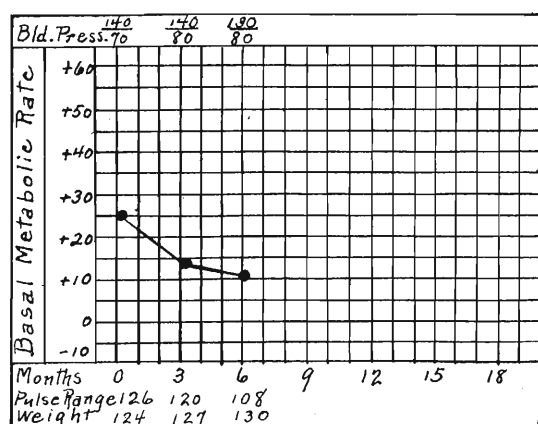
We are positive that no one treatment will control all cases of toxic goiter, but

that after defining and correlating the symptoms and classifying the case pathologically, the indications for treatment should be manifest.

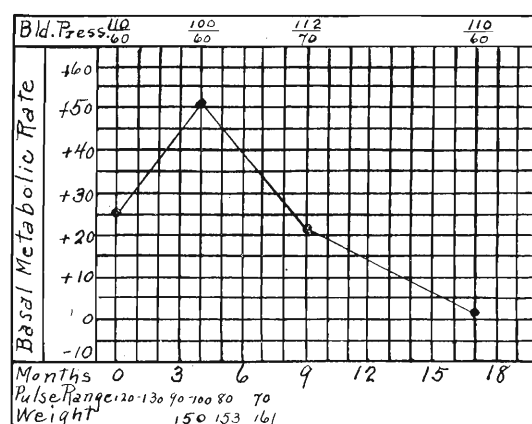
Furthermore, special consideration must be given to the associate or subsidiary symptoms before and after treatment. It is generally agreed that rest and quiet are helpful factors. An ice bag may be applied to the gland and precordium. Plenty of easily digested food, tepid baths and alkaline drinks are equally important. Digitalis as a therapeutic splint to an irregular, rapidly beating, dilated and decompensated heart, will sometimes tide over a catastrophe. Blood transfusion is

Leniency must be used in the criticism of scientific men who, ignoring radium entirely, assert that all treatments have failed except surgery. It must be remembered that prejudice and inexperience will warp the soul of the most sublime.

Radium therapy for toxic goiter as standardized and given to this Society by the author two years ago, at the Boston meeting, merits your serious interest. After seven years of experience with the element, the last three under the most exacting scrutiny by means of laboratory methods and clinical findings, I conclude that toxic goiter can be cured by radium and that it is *not* a surgical disease.



CASE 806. August, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 603B. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

indicated in a low cell count, 30 per cent or lower hemoglobin and general edema, and more especially when the toxemia has been profound enough to produce a severe psychosis. Bromides and ergot have their place in assisting in the control of certain symptoms.

It was through the efforts of the surgeon that we began to realize the importance of the present conception of the disease. For this reason, therefore, surgical findings in toxic goiter should be held in the highest regard.

Without consideration of the surgical mortality in the most skilled clinics, we must consider this great danger in other centers; also the fear, apprehension, hospitalization and financial cost to the individual, not forgetting the possible return of all symptoms.

Of the 180 cases I have treated, only 10 were subjected to a second radiation. Four of these had large cystic adenomata and the toxic activity was not completely controlled after the first treatment. The other 6 were given the second treatment with the hope of further reducing the enlarged gland. Three cases, in a state of extremus from myocardial degeneration with general edema, died. One insane patient died from starvation before the treatment had time to benefit the toxemia.

Improvement is noted within the first ten days after treatment, but about the third week all the old symptoms may return, due to the radium reaction. This active stage varies in different individuals. Some express disappointment in not feeling

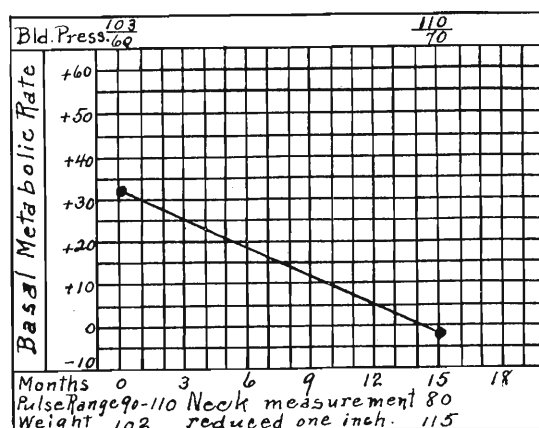
bad, while others are nauseated for a few days.

Within four weeks the nervous tremor has commenced to subside, the appetite has improved and the heart has slowed down twenty or thirty beats. After two months all the symptoms are much better and most individuals gain a few pounds in weight. The improvement is gradual, as shown by the cases reported when the metabolic rate has been taken every three months after treatment.

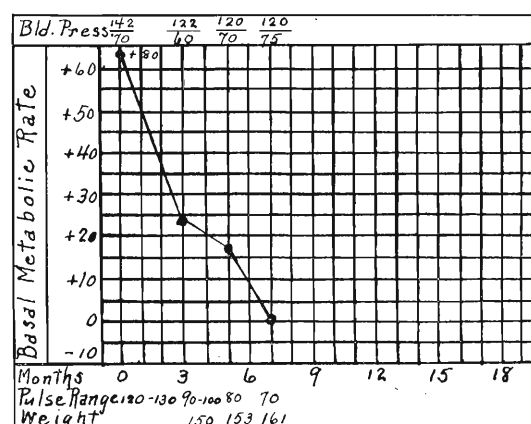
Some cases are free from all symptoms after six months, while others with large adenomata of long standing and with extensive myocardial change take twelve

these young women they run an active and rapid course, so that the symptoms are grave in a very few months. Sixteen of these cases have been treated, and 10 have had second and third pregnancies since treatment without any evidence of thyroid toxemia. Two showed activity at the beginning of lactation but were controlled by means of the ice bag.

Two of our cases had two operations each and 8 had one each for thyroidectomy. Four others had ligation of the thyroid arteries on one side and 2 had both superior thyroid arteries tied off. They had all been benefited for a period of six months to two years, but the remaining portion



CASE 720. October, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 604. February, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

to eighteen months to show a normal metabolic rate with a normal heart action.

The enlarged gland gradually decreases in size in direct relation to the amount of cystic formation present. All hypertrophy or hyperplasia is reduced to normal while the cystic type is reduced about one-half in size. The exophthalmus in many of my cases has been controlled after three years. However, all do not respond so favorably.

There has been no evidence of myxedema in any of the cases treated. Metabolic readings have been made over a period of two and a half years and all have remained normal.

Many toxic adenoma cases give a history of pregnancy, childbirth or miscarriage initiating the toxic activity. In

of the gland had hypertrophied and soon became active. On account of parathyroid glands, discretion in the technique of treatment of postoperative cases must be used.

None of my cases have shown any symptoms of parathyroid dysfunction after treatment.

For the last two years all cases with infected tonsils associated with a toxic thyroid have received treatment over the tonsil area conjointly with that of the thyroid gland. One case had a gall-bladder drainage and two had operations for chronic appendix six months after the thyroid treatment.

Abdominal support is given all cases that show visceroptosis by roentgenography. It has been shown experimen-

tally that stimulation of the cervical sympathetic nerves in animals produces exophthalmic goiter, and that thyroid secretions lower the threshold to sympathetic stimulation, so that a vicious circle is established.

It is a question whether radium therapy breaks the vicious circle by diminished gland secretion, thus restoring the balance by some specific effect of the rays on thyroxin itself, or whether radium acts mechanically by blocking the blood supply.

The rapid control of the toxic symptoms after treatment would support the hypothesis of a change in the character of the secretion. Diminished secretion due to

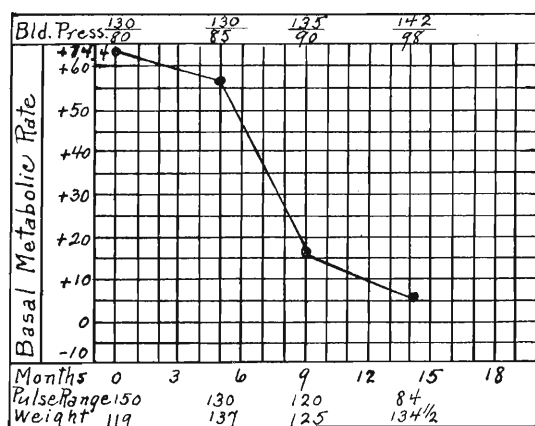
physiological dystrophies of the thyroid toxemia.

SIGNS AND SYMPTOMS IN EXOPHTHALMIC GOITER

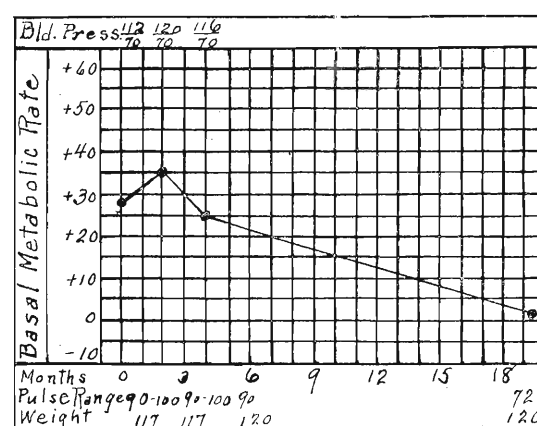
It certainly must be more than a mere coincidence that the signs in exophthalmos so closely approximate the phenomena which result from the experimental stimulation of the inferior sympathetic cervical ganglia. These signs have been produced in dogs and have also been observed singly or in combination in man when these ganglia were stimulated or irritated.

Let us notice, therefore, the anatomical and physiological mechanisms associated with these ganglia and their accompanying phenomena.

1. There is a sheet of involuntary muscle in the upper lid which is supplied by filaments



CASE 741. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 611. February, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

cellular change would come later, while thrombosis of the smaller arterioles and capillaries would come last of all.

Corroboration of the objective and subjective symptoms by laboratory standards will verify the findings and establish the diagnosis. The basal metabolic rate in thyroid toxicity proves more than clinical findings, as it registers the degree of severity as shown by the variation in records. A +60 case indicates greater activity, toxicity and severity than one of +20. This known difference in rate is a helpful factor in the prognosis of the case.

I wish to present here the comprehensive and forceful opinion of C. F. McClintic, M.D., Professor of Anatomy, Detroit College of Medicine, explaining many of the anatomical changes and

from the cervical ganglia. When this muscle (Mueller's) is stimulated to contraction the upper lid becomes narrowed, the lid rises above the upper margin of the cornea and exposes the white sclera and results in a widening of the palpebral fissure. This accounts for the signs of Graefe and Stellwag.

2. Stretched across the sphenoidal fissure in the apex of the orbital cavity is a sheet of involuntary muscle, the orbicularis muscle, which is supplied by sympathetic nerves from the above ganglia. When this muscle contracts it pushes forward the contents of Tenon's capsule and thereby causes protrusion of the eyeball, or exophthalmos.

3. In the orbicularis oculi and musculature of the forehead are strands of involuntary muscle which, when stimulated, prevent wrinkling of the skin of the forehead. This musculature is supplied by the sympathetic ganglia of the neck. This mechanism explains Joffroy's sign.

4. (a) From these ganglia arise the accelerator nerves to the heart; their stimulation therefore increases the force and rate of the heart tachycardia, and thus raises the blood-pressure.

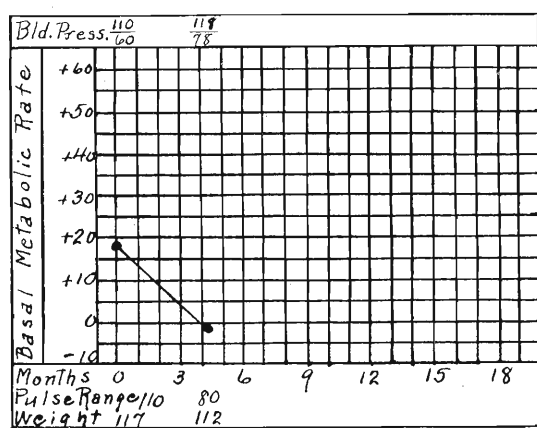
(b) The disturbance of the heart and vasomotor centers assists in explaining the gastrointestinal and toxic symptoms.

5. The sympathetic nerve when stimulated increases the capacity of the respiratory tree, and the chest remains full (therefore expansion is more limited). This increase in lung capacity with the circulatory changes will explain the findings in basal metabolism.

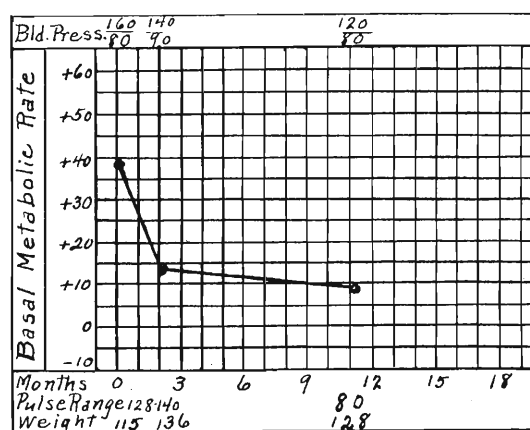
6. The vasomotor nerves to the head, face, neck and upper limbs arise from these ganglia and thereby account for sweating and other vasomotor phenomena. It has been

section that filaments of the sympathetic encircle the inferior thyroid artery. When, for any reason, the diameter of the artery becomes increased it tugs upon the nerve and thereby irritates the ganglion, the irritation stimulates the ganglion, it in turn stimulates the heart to force more blood through the artery, this again increases the tugging on the ganglion, etc., thus initiating a vicious circle which can produce all the signs of the condition. May this not account for Osler's cases which occurred from fright and soon passed off?

10. Changes in the gland may occur as a result of the disturbance of its nutritional mechanism. The disturbances or irritation of the ganglia may result from (a) pressure due to enlargement of the thyroid gland, (b) increase in the diameter of the inferior thyroid



CASE 833. October, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 687. July, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

demonstrated experimentally, that these areas are intimately connected with those of the lower extremity.

7. The tremor and rhythm are the same as those for smooth muscle. Langley¹ has shown that all voluntary muscle is supplied by the sympathetic. This will explain how the irritation of these ganglia will account for the tremor. It also explains the sign of Moebius.

8. The bruit associated with exophthalmos and enlarged thyroid is accounted for by the relations of the gland to the common carotid artery. The enlarged gland presses upon and constricts the lumen of the vessel. The blood rushing through the narrowed lumen into the larger portion produces the bruit.

9. The pulsation of the gland may be due to increase in the flow of blood through the inferior thyroid arteries since the gland acts as a shunt to prevent too much blood reaching the brain. It is interesting to note in this con-

nection that filaments of the sympathetic encircle the inferior thyroid artery. When, for any reason, the diameter of the artery becomes increased it tugs upon the nerve and thereby irritates the ganglion, the irritation stimulates the ganglion, it in turn stimulates the heart to force more blood through the artery, this again increases the tugging on the ganglion, etc., thus initiating a vicious circle which can produce all the signs of the condition. May this not account for Osler's cases which occurred from fright and soon passed off?

11. Fitting in with these facts is the adrenalin test for exophthalmic goiter. It is to be expected that the administration of adrenalin will aggravate all of the above-mentioned phenomena.

The writer merely mentions these facts as a possible explanation for the signs in exophthalmic goiter based on the functional mechanism associated with the cervical sympathetic ganglia.

RADIUM TREATMENT

At least 100 mgm. of element are used (more often I use 130) in four tubes, each tube being screened in one mm. of brass and 1 mm. of gum rubber. To obtain distance, the screened tubes are placed 1 cm. apart on a gauze pad 2 cm. in thickness.

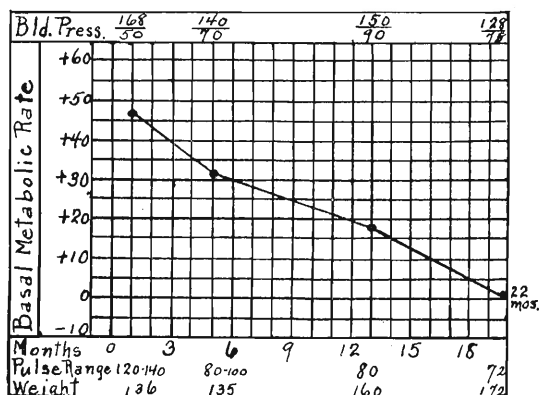
The gauze pad is made with a loop of adhesive tape at each end so that it can be adapted and tied over an uneven surface without strapping. The radium pad is placed over one lobe for eight or ten hours and then over the other for an equal time, depending on the size of the lobe and the amount of radium used. If the isthmus is enlarged the pad can be ar-

gestion, diarrhea, etc., until the therapeutic effect of the radium has been established.

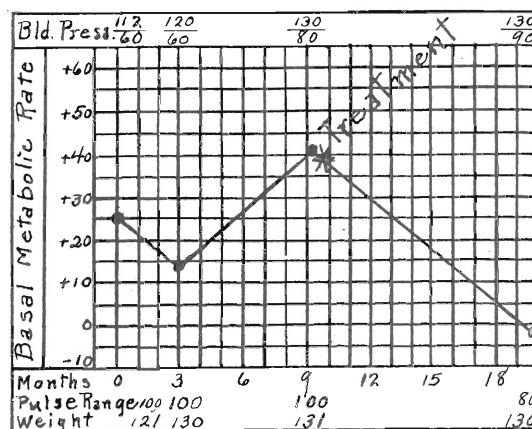
CASE 726. Jan. 29, 1921. Female, aged thirty-one years; married; mother of one child eight years of age.

Family History. Negative.

Past History. Had measles and small-pox when a child. Menstruated at thirteen years; always regular. Had a left brachial cyst removed when seventeen, also had tonsillectomy. Had an ovarian cyst removed five years ago. For the last two years she has had "throat trouble." Had difficulty in breathing and, when going up stairs, tracheal pressure. Severe headaches; fatigue and disinclination to work. Perspires freely and at times has one or two degrees



CASE 599. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 726. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

ranged to cover one side of it at each application without overlapping and endangering the trachea.

This technique in treatment will give an active hyperemia in the blonde type of individual. The susceptibility of some people (especially if there is a vasomotor disturbance like sweating) has to be considered; so that judgment must always be used at all times.

It is well to advise the use of the ice bag in hourly periods each day, over the gland, for a few weeks following the treatment. This insures rest and controls circulatory and cellular activity. As mentioned before, subsidiary treatment is important after radiation to control arising symptoms of insomnia, tachycardia, indi-

of fever. Appetite good; bowels regular; no insomnia. Has had some middle-ear disturbance from Eustachian infection.

Examination. No eye manifestations. Fragments of lymphoid tissue within the pillars of both tonsils so that the posterior pillars are adherent to the pharyngeal walls and show evidence of infection. The thyroid gland is enlarged; not cystic, but soft, and causing a compression of the trachea. The left lobe extends beyond the sternomastoid muscle and adjoins the brachial cyst keloid scar. The right is also enlarged but lies well behind the muscle. The area of heart dulness is normal in outline and no murmurs are detected. Pulse rate 110; blood-pressure: systolic 130, diastolic 80. Metabolic rate plus

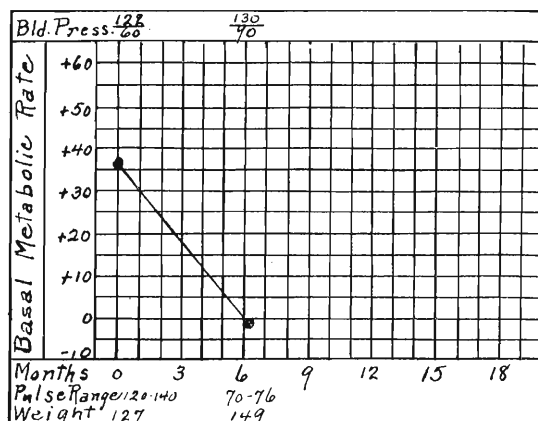
24.1. Upper circumference of neck $13\frac{3}{4}$; middle $14\frac{1}{4}$; lower $14\frac{3}{4}$ in. There is a tremor of fingers on extension; nails have longitudinal striae.

Diagnosis. Toxic adenoma.

Treatment. Local treatment for throat; rest; ice bag to neck with quinine hydrobromid medication.

April 23, 1921. Throat much better, with some improvement in general symptoms. Metabolic rate today plus 13.5.

Oct. 7, 1921. Improvement was only temporary, so that now all the symptoms are exaggerated. Headaches worse; tachycardia; pulse 120; some diarrhea. Metabolic rate plus 40.4. Recommended radium treatment.



CASE 810. August, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

Nov. 2, 1921. One hundred mgm. radium element were used with previously described technique over each lobe of the thyroid for ten hours, and 40 mgm. in the same screening held behind the jaw over each tonsil area for ten hours.

The patient made a satisfactory recovery with complete alleviation of all symptoms. She moved to another city so that I was unable to follow the course of the improvement.

Dec. 7, 1922. After fourteen months of complete relief from all the old symptoms the scar on the side of the neck has softened down and both lobes of the thyroid are apparently normal in size. The lymphoid tissue at the site of the right tonsil has disappeared and the left is healthy in

appearance. Pulse rate 80; full and regular. Systolic blood pressure 122; diastolic 80; metabolic rate minus 2.1.

CASE 810. Aug. 11, 1922. Male, aged thirty-nine years; married; brakeman. Complained of shaking of the hands, legs and body and of fatigue.

Family History. Negative.

Past History. When thirty years of age he had a renal colic and passed a calculus. Two years ago he was in a railroad accident and had his left clavicle and three ribs broken, also both shoulders injured. He was laid up for five weeks and was very nervous for three months following. About a year ago he had influenza.

Present Illness. Three months ago he became shaky in the limbs, weak, tired easily, was nervous, had insomnia and would wake after sleep with a feeling of fulness in his head. Would almost faint at times from weakness and palpitation.

Examination. Right eye slightly larger than the left. No other eye symptoms. Tongue tremulous. Both tonsils enlarged and chronically infected. Tonsil crypts were filled with necrotic material. Throat and soft palate injected from smoking. Teeth in good condition. Neck very slightly enlarged. Left lobe of thyroid larger than right. Isthmus normal. Some pulsation in neck but no bruit heard. Heart dilated with apex in nipple line. Heart sounds rapid, but no murmur detected. Tremor of hands and knees. Nails have longitudinal striae. Radial pulse 100; apex beat 120; systolic blood pressure 122; diastolic 90; metabolic rate, plus 36.1.

Diagnosis. Primary exophthalmic goiter.

Prognosis. Good; should be controlled.

Treatment. (1) 60 mgm. radium element in 1 mm. brass and 1 mm. rubber and $1\frac{1}{2}$ cm. gauze was held beneath right ear over tonsil area for seven hours. (2) 100 mgm. in 1 mm. brass, 1 mm. rubber and 2 cm. gauze in form of a pad was held over left lobe of thyroid for seven hours. (3) The same packages were held over the right tonsil area and thyroid lobe for eight hours.

Sept. 14, 1922. Present weight 133 lbs., or a gain of 6 lbs. since August 11th. Has been feeling fine. Complains of some

palpitation and precordial heaving after eating and vigorous exercise. Has had no sore throat or distress of any kind; toxic symptoms lessened greatly.

Examination. Throat and mouth still injected from smoking. Tonsils small with some infection in the left one; neck not enlarged. Heart sounds normal. Pulse and apex beat 100. Systolic blood pressure 130; diastolic 60; metabolism not taken.

Feb. 12, 1923. The patient was treated six months ago. Has never felt better in his life; complains of rapidity of heart action on exertion only. Examination showed the eyes normal; color good; neck still small with no evidence of enlargement or local effect of treatment. No tremor; all symptoms controlled. Present weight 149 lbs., or a total gain of 22 lbs. Pulse rate 74; systolic blood-pressure 130; diastolic 70. Metabolic rate minus 3.9.

CASE 805. July 13, 1922. Female, aged thirty-nine years; married; housewife. Complained of choking sensation and general weakness.

Family History. Negative, except that her mother had goiter.

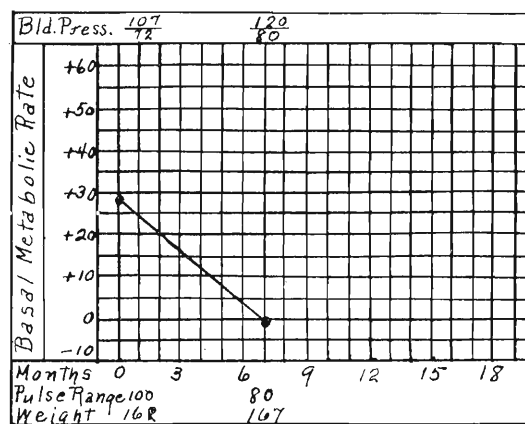
Past History. Had children's diseases. Always been more or less anemic. At the age of six years the thyroid gland enlarged but became smaller after puberty. Gave no evidence of activity until after the birth of her first child. When lactation ceased the activity subsided until after her second child was born. The activity persisted this time and she was compelled to have a complete left, and a partial right, lobectomy performed three years ago. All symptoms subsided and she remained well for over a year. The gland commenced to enlarge gradually but without any symptoms until about a month ago when she had an acute attack of tonsillitis.

Present History. The patient finds it difficult to breathe at night when lying down, so has been compelled to sleep in a sitting position for nearly three weeks. Has a choking sensation in stooping over or on exertion. Is weak, fatigues easily and is disinclined to work.

Examination. Left eye full and more staring than the right. Right eye also prominent but shows less sclera than the left. Both tonsils enlarged, injected and

appear infected. The tongue is tremulous. The neck shows a circular scar down near the clavicle with a bulging prominent right lobe of the thyroid, and an enlarged cystic isthmus. The mass as a whole forces the trachea toward the left and holds it backward, accounting for the choking sensation with increased blood pressure in the head. Upper circumference of the neck is 15 in., middle 15½, lower 16. Heart sounds normal; no murmurs detected. Apex beat and pulse registering 90; systolic blood pressure 107; diastolic 72; hemoglobin 65 per cent; metabolic rate plus 29.0. Some tremor of the hands and fingers.

Diagnosis. Toxic adenoma, recurring as a result of acute tonsillar infection.



CASE 805. July, 1922. Comparison of B.P., B.M.R. pulse range and weight in months after radium treatment.

Treatment. Ninety mgm. radium element in four tubes screened as before, made into a pad 2 cm. in thickness and held over the right lobe and isthmus for twelve hours. Eighty mgm. in two packages of 40 mgm. each with same screening was held below the ear and behind the jaw over the tonsil areas on each side for ten hours.

Feb. 3, 1923. It has been nearly six months since the treatment. The patient reports that within a month she began to improve and that now she feels well has no nervous symptoms, choking spell or other discomfort.

Examination. Patient looks much better. Right eye still full; right tonsil small; left red and injected. Right lobe and isthmus smaller and measurements show a decrease of 1 in. in each of the two upper

rcumferences, and $1\frac{1}{2}$ in the lower. land soft, and very little tension in the ystic isthmus. The pulse rate is 78; ystolic blood pressure 112; diastolic 80; emoglobin 85 per cent; metabolic rate minus 2.2. The patient has gained $3\frac{1}{2}$ lbs. weight.

May 16, 1923. At the present time here is no evidence of thyroid toxicity xcept the fulness of one eye; and the atient reports feeling very well with none her old symptoms present.

CONCLUSIONS

1. A high systolic and a low diastolic blood pressure show a normally balanced

pulse pressure in some cases before the metabolic rate becomes normal.

2. Three months after treatment the metabolic rate was found to be normal in many cases that had been active.

3. A high systolic blood pressure in the late stages of a toxic adenoma is conclusive evidence of myocardial or renal degeneration whenever it is not reduced 20 or 30 per cent after the normal metabolic rate has been re-established.

4. The basal metabolic rate proves and estimates the degree of thyroid activity and also furnishes conclusive evidence of toxic control after radium therapy.

THE RADIUM TREATMENT OF VERNAL CONJUNCTIVITIS



BY

HARRY H. BOWING, M.D., AND ROBERT E. FRICKE, M.D.

Reprinted from
The American Journal of Roentgenology and Radium Therapy
Vol. XXXVIII, No. 5, November, 1937

THE RADIUM TREATMENT OF VERNAL CONJUNCTIVITIS*

By HARRY H. BOWING, M.D., and ROBERT E. FRICKE, M.D.

Section on Therapeutic Radiology, The Mayo Clinic

ROCHESTER, MINNESOTA

VERNAL conjunctivitis or vernal catarrh is an exceedingly distressing and disabling malady but, fortunately, radium therapy can, in most cases, cure or shorten the duration of the disorder. The disease has long been recognized and any standard textbook on ophthalmology details the symptoms, course, and pathology, describing the cobblestone or pavement-like appearance of the hypertrophied papillae of the affected conjunctiva.¹ The true etiology is unknown. Many remedies, such as boric acid, salicylic acid ointment, corrosive sublimate, and so forth, may ameliorate the symptoms without altering the underlying pathologic condition.

Microscopically, the process is apparently one of penetration of the cellular and vascular stroma by strands of epithelial cells projecting from the thickened plaques of epithelium so characteristic of this disorder. The therapeutic rays of radium affect the radiosensitive cellular infiltration and connective tissue elements of the lesion. Since hyaline degeneration occurs normally in the stroma and it is known that this process can be definitely accelerated or enhanced, it seems best to avoid all possibility of overtreatment.

Radium has been used for this condition since the advent of radium therapy and it is regarded by many as a specific. In 1910, Sir J. Mackenzie Davidson reported cures of this disease, one dating back to 1906. The reporting of cures, however, is of doubtful value because the disorder will usually clear up spontaneously after a few years. The relief afforded by careful treatment and correction of the underlying condition is of great value and comfort to the afflicted patient.

This study which was in part inspired by the excellent paper on the subject by Pendergrass and Andrews, read before this So-

ciety two years ago, is a brief analysis of the cases of patients with vernal conjunctivitis seen at The Mayo Clinic during the five-year period from 1931 to 1935, inclusive. During this period 23 patients were treated by radium.

ANALYSIS AND RESULTS

These 23 patients proved to be older, and the disease of longer standing, than the group presented by Pendergrass and Andrews. Seventeen of our patients were males, 6 females. The youngest patient treated was three years old, the oldest thirty-six. Their average age was eighteen years. The symptoms were typical and consisted of lacrimation, photophobia, burning, itching, pain, and often impairment of vision. The longest duration of the conjunctivitis was twenty-three years, the shortest four months, the average duration being six years. In practically all cases the condition has been modified by previous treatment, such as various forms of medication or desiccation, curettement of granulations, and so forth. The number of radium treatments varied from only one, in 6 cases, to eleven; the average number of treatments was three.

The relationship of the disease to allergic phenomena is interesting both from the etiologic and therapeutic standpoints. Of the 23 patients, 5 displayed definite allergic manifestations. Three patients were sensitive to certain types of foods, 2 to pollens and grasses. Three of these 5 patients showed definite improvement following radium treatment locally, dietary instruction and desensitization to offending pollens; these patients were children, aged six and nine, respectively, and one adult, aged twenty-one. The two other sufferers obtained no relief whatever; both were adults, one being sixteen years of age and the other

* Read at the Twenty-second Annual Meeting, American Radium Society, Atlantic City, N. J., June 7-8, 1937.

FIG. 1. Five, 20 and 25 mg.
radium plaques.

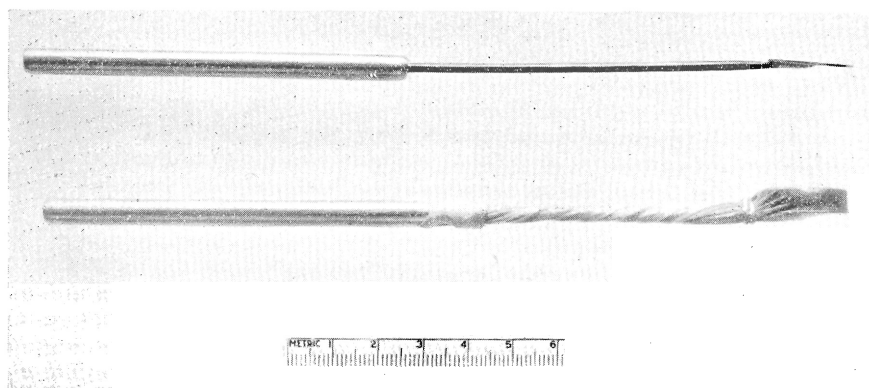
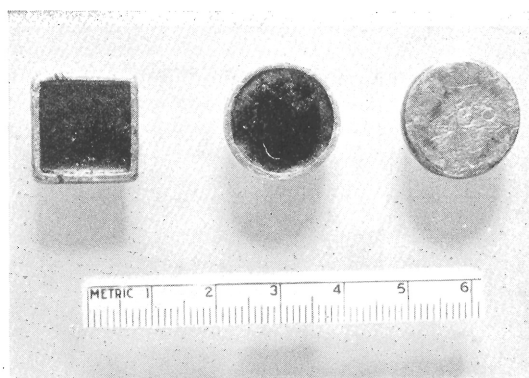


FIG. 2.
Applicator
ready for
use.

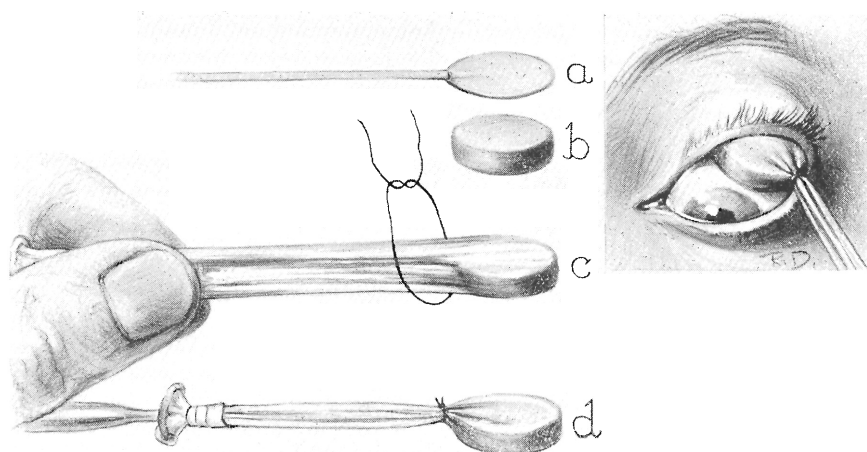
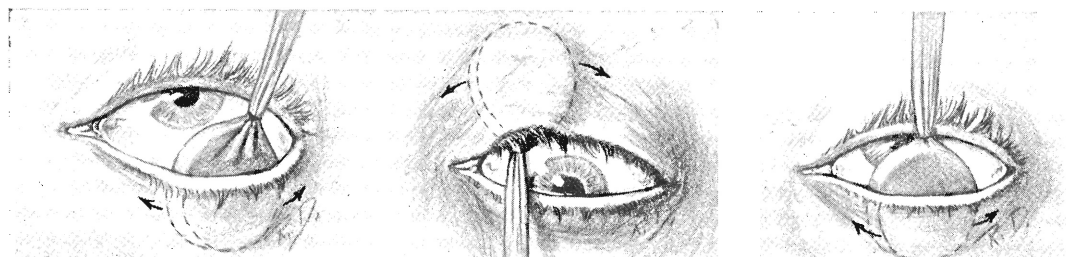


FIG. 3. Applicators: *a*, holder; *b*, radium plaque; *c* and *d*, application of
rubber finger cot to hold plaque in place: treatment of upper half of globe.



twenty-eight. Each had only one radium treatment. The three who obtained successful results had two to five radium treatments each.

Returning to the entire group, both upper and lower eyelids were involved and were treated in 12 cases. In only 3 cases were the upper lids alone affected, and in only one case the lower lids. The conjunctiva of the globe was diseased and treated in 7 cases, both upper and lower lids usually also being involved. In only one case was the globe alone affected, and in 2 cases only the globe and upper lids were affected. Mechanically, the globe and lower lids are more difficult to treat adequately than the upper lids. Of our 5 failures, 3 were in the small group of cases in which the globe was involved.

The results of treatment in these 23 cases were good in 18, or 78 per cent, eventuating either in cure or marked improvement. No improvement occurred in 5 cases, or 22 per cent.

TECHNIQUE

Treatment of the delicate structures involved is tedious and the results vary with the degree of care employed. Avoidance of corneal ulceration and scarring and loss of cilia are important. In all 23 cases beta radiation derived from plaques of radium sulphate (element) containing 5, 20, or 25 mg. was employed. These plaques were small, being about the size of a five-cent piece (Fig. 1); in the case of the first two plaques, the filter used was just varnish. For the third plaque the filter was a thin leaf of 0.1 mm. monel metal. For treatment of the lids or bulbar conjunctiva we have devised a very thin metal holder in which the plaque is attached by means of a very thin, rubber finger cot. The orbital tissues are anesthetized by 3 or 4 drops of a 5 per cent solution of cocaine, 1 drop being instilled every two or three minutes. The plaque on the metal applicator (Figs. 2 and 3) is lubricated with a coating of white vaseline. The plaque is then kept moving over the involved area for the requisite time, the metal back of the plaque serving

to protect the tissues not undergoing treatment. The dosage with each of the three plaques has been ten minutes per area, an area consisting of the entire affected upper lid, or lower lid, or the bulbar conjunctiva. Thus if both eyes and the upper and lower lids and bulbar conjunctiva were involved, the entire treatment would consume sixty minutes. Individual treatments were spaced at least three months apart (Figs. 4, 5 and 6).

SUMMARY AND CONCLUSIONS

Vernal conjunctivitis, while fortunately rare, is a very disabling and painful disease. Radium treatment is effective in most instances, and demands usually two or three cautious applications of radium at intervals of a few months. Happily, in most cases, the lids alone are involved. When the conjunctiva of the globe is also affected, the disease is more widespread and the results are often not as good.

Apparently irradiation has a marked corrective effect on the underlying pathologic condition. Short individual treatments with beta radiation, employing practically unscreened radium element, appear to be effective. These treatments must be gently and cautiously given. The important fact which needs constant emphasis is that one is dealing with a benign disease which will usually heal spontaneously after a few years. Hence the greatest care is essential that no injuries arise from treatment. Ulceration of the delicate tissues treated, with subsequent scarring or loss of cilia, must be avoided.

REFERENCES

1. MAY, C. H. *Manual of the Diseases of the Eye*. Ninth edition. William Wood & Co., New York, 1919, pp. 127-129.
2. DAVIDSON, J. M. Quoted by Williams, F. H. *Radium Treatment of Skin Diseases, New Growths, Diseases of the Eye and Tonsil*. The Stratford Co., Boston, 1935, p. 37.
3. PENDERGRASS, E. P., and ANDREWS, J. R. The radium emanation treatment of vernal catarrh. *AM. J. ROENTGENOL. & RAD. THERAPY*, 1935, 34, 637-640.

CANCER DESTRUCTION BY RADIUM

By JOSEPH B. BISSELL, M.D., F.A.C.S., New York
Visiting Surgeon, Bellevue and St. Vincent's Hospitals

Reprint from
SURGERY, GYNECOLOGY AND OBSTETRICS
July, 1915, pages 98-102

nical proofs of this action of radium are illustrated in the following cases. For the purpose of this paper those only have been selected in which the tumors have been proved by pathological examination to be malignant and in which, under treatment, the growth has disappeared.

CASE 1. J. S.; farmer; age 61; March 21, 1914. Patient has basal-celled epithelioma of the neck, recurrent. Has extensive and deep ulceration extending from the root of the ear down the neck. Part of the lobe of the ear is destroyed. The ulcerated surface is about three by two and a half inches in extent. The large vessels of the neck are exposed. Besides two previous operations the ulcer has been recently thoroughly cauterized. Forty milligrams of radium applied for 9 hours. April 10, 40 mg. of radium applied for 9 hours. April 16, 40 mg. of radium applied for 9 hours. April 23, the lobe of the ear is entirely healed and covered over with new skin, and the ulcer is reduced to about half an inch in diameter, which is healing rapidly. Forty milligrams of radium applied for 12 hours, and the patient left for his home the next day, writing me at the end of two months that the ulcer is entirely healed and that there was no further use for radium. He received in all 1,560 mg. hours of radium the course of his treatment.

CASE 2. J. F. F.; storekeeper; age 57; October 9, 1914. Patient has a lump about the size of a small orange involving the upper part of the sternum at its junction with the clavicle extending posteriorly into the mediastinum and anteriorly into the right cervical region. Three weeks previously a tumor of this size had been removed by operation and the wound had healed kindly and rapidly. Recurrence began about a week afterward. Pathological report as to tumor was that it was a carcinoma. Today 100 mg. was applied, properly screened, over the region allowed to remain for 20 hours, patient going to his home in the country next day. October 16, he returned complaining of a slight burning of his skin, but with the tumor reduced to about half its size. October 29, skin is still very tender, but the tumor has almost entirely disappeared. November 12, very slight evidence of tumor remaining, but he has two well-marked radium burns; one over deep eschar about an inch in diameter and another over half an inch in diameter, both painful and discharging; — one to the right and the other to the left of the upper border of the sternum. December 10, the two sides of the sternum and each clavicle in the sternum region appear to be similar and normal. No evidence whatever of any tumor. The skin is still tender over the burned regions. Patient discharged. One radium application of 2,020 mg. hours.

CASE 3. Mrs. S.; age 40; housewife; seen September 10, 1914. History of carcinoma of the breast of two years' standing. Breast removed November 10, 1913. Small nodules scattered around the wound and in the surrounding skin; recurred in May, 1914. The pathologist's report was adenocarcinoma of the right breast. At this time 101 mg. of radium applied in divided tubes for 30 hours over a circle of about six inches in diameter. October 1, well-marked radium burns present, but healing; none of the nodules have disappeared, but as the induration along the wound is still marked another application of radium was advised but refused on account of the burns. November 2, radium burns still present but slowly improving. A number of new-skin nodules have appeared outside the circumference of the others. One hundred and one milligrams of radium applied for 15 hours. December 6 radium burns still severe. One large burn on

her side over a recent nodule is very deep and troublesome and is about an inch and a half in diameter, excavated and quite painful. One hundred and one milligrams of radium applied for 9 hours, changing the location of the application every hour. December 19, condition about the same except that some of the burns are healed. There are present at least a hundred nodules, some of them quite large. One hundred and one milligrams of radium applied for 22 hours, changing the site of the application every two hours. The radium was screened by 8 mm. of felt as well as by 0.5 mm. of lead. December 23, nodules are slowly disappearing and only one of the large ones remains. February 5, 1915, patient is improving. Most of the burns have healed. The large burn posteriorly is still present, but the induration underneath it has gone, as have apparently most of the other nodules. Patient's general condition is very much improved. She has increased in weight, has better color and appetite, sleeps well, and is quite contented with her condition. One hundred and one milligrams applied to various parts of the lesion for 20 hours. April 15, patient has had two applications of radium of 101 mg. for 20 hours each time since the last note. The nodules have all disappeared except two or three suspicious spots in place of the hundred and more indurations she had when the treatment began. Two small radium burns still persist. Ninety milligrams of radium applied for 20 hours to the suspicious points. In her treatment this patient received in all 5,536 mg. hours.

CASE 4. Madame L. D.; age, 69; occupation, governess. Patient gave a history of having had a laparotomy for removal of a tumor of the uterus seven years ago. Six months previous to my seeing her she had a tumor removed from her back, which the pathologist reported to be a round-cell sarcoma. One month later recurrence took place. On admission to the hospital, at the site of a scar over the border of the left scapular spine, at its inner extremity, was seen a small ulcerated growth with characteristic odor. This, the patient stated, had been present for about two weeks. On February 26, 1914, this growth was removed together with the remaining scar-tissue. This was reported by the pathologist to be sarcoma. The operation wound healed kindly, but on March 10, as there seemed to be some tendency to infiltration of the skin at this point, 40 mg. of radium element were applied for 2 hours. After the first application there was no further discharge; the induration and slight tendency to ulceration which had been present disappeared; there was no further pain or irritation of any kind, and the site of the operation wound was apparently normal except for a white scar line. Examination on May 10 showed no evidence of any return of the growth, but 40 mg. of radium were again applied for 2 hours. April 10, 1915, there was no return of the growth. This patient received in all 1,120 mg. hours.

CASE 5. J. McE.; age, 55; occupation, waiter; August 27, 1914. Twelve days ago the patient first noticed a tiny abrasion inside the lower lip to the right of the middle. On September 30 this had increased to the size of a large pea. October 20, the whole lesion was excised and the wound sutured. The pathologist's report was sarcoma. October 21, 20 mg. of radium in two tubes were applied for 1 hour. October 23, the wound appeared entirely healed and stitches were removed. October 29, lip was apparently normal. Incision had healed by first intention. Thirty-six milligrams applied for 30 minutes. November 12, 20 mg. were applied to the inner surface of the lip and 26 mg. to the outer, over the line of the incision, for 40 minutes. December 10, 20 mg. in two tubes applied for 40 minutes. The line of incision has practically disappeared. There has been at no time any local reaction.

April 5, up to date there has been no return of the tumor. This patient had 550 mg. hours.

CASE 6. Rev. C. McC.; age, 70; occupation, ecclesiastic; December 26, 1914. This patient has growth in front of left ear, raised three-quarters of an inch above skin surface and about one-half inch in its longest direction by three-eighths of an inch in width, with superficial ulceration. This tumor has been growing for several months. Without removal 10 mg. of radium was applied for 20 minutes. December 30, no apparent reaction of the skin or tumor. The growth was removed with curved scissors under local anæsthesia and immediately afterwards 50 mg. of radium was applied to the excavated base. Examination proved it to be epithelioma. January 27: Since the removal of the growth he has made weekly visits and 10 mg. of radium have been applied each time for 10 minutes. February 8, growth seemed to be slightly filling in from the bottom. Twenty-five milligrams of radium were applied for 10 minutes. March 10, up to date 10 mg. of radium for 10 minutes each visit have been applied for four visits since the last report. The ulcer has been completely destroyed and new skin is running in from the edges. There is no evidence of radium burn. April 6, patient called for observation. There is no change in the condition. Patient was told to return in a couple of months to see if further treatment was necessary. April 11: He died this morning of a sudden attack of pneumonia. In all this patient had 3,200 mg. hours' treatment.

CASE 7. F. W.; age, 16; school girl; March 17, 1914. Patient has suffered for several months from enlargement of the left lower jaw and adjoining lymphatic glands. Pathological examination of one of the glands showed it to be sarcomatous tissue of spindle-celled variety. Forty milligrams of radium applied in divided doses for 4 hours. March 20, no local reaction from the preceding treatment; the swelling of glands and jaw was markedly lessened; 40 mg. of radium again applied for 4 hours. Two weeks later the patient appeared to have entirely recovered. There was no irritation or redness of the skin over the tumors. April 17, 1915, the patient's mother reports that patient is entirely well. She had 320 mg. hours.

CASE 8. F. C.; age, 42; occupation, broker; October 17, 1914. Patient has epithelioma of the floor of the mouth involving the lower jaw at the median line. This tumor was removed and the pathological report confirmed the diagnosis. October 22, 45 mg. of radium applied for 10 hours in divided doses to the inside and outside of the jaw, one tube of 25 mg. being applied 10 hours under the tongue close to the median line. October 29, under surface of the tongue somewhat inflamed and tender. Ten milligrams of radium, well screened, applied to the under surface of the tongue at affected point and 51 mg. to the under surface of the chin for 4 hours. November 12, no return of the tumor noticed, but there is a slight tenderness and superficial swelling at the root of the tongue behind the teeth, at the site of the cicatrix. Skin on the under surface of the chin is red, tender, and scaling. No radium applied on account of tendency to burn. February 9, 50 mg. applied for 22 hours to the under surface of the chin. On account of a well-marked burn on the under side of the tongue no radium is applied on the inside of the mouth. April 4, 1915, the radium burns have all disappeared and there is no evidence of any return of the growth. He has a slightly enlarged and tender lump in the middle line behind the prominence of the chin. Seventy-one milligrams of radium applied to this point for 8 hours. This patient had in all 2,662 mg. hours of treatment.

CASE 9. J. W.; age, 51; occupation, ship's carpenter. This patient had epithelioma of the eyelid. Eleven

years ago he was operated upon for a similar tumor said to be malignant. The present tumor was removed, and pathologist's report showed it to be epithelioma. After excision the wound was united by three stitches, which parted on the third day, leaving a gaping wound. This was resutured, and at the same time 10 mg. of radium were applied for 20 minutes. No evidence of radium burn was noticed from either of these applications. At the end of three weeks from the first operation 10 mg. of radium were applied again for 20 minutes and the patient was discharged. This patient had 600 mg. hours' treatment. No recurrence when seen April 20, 1915.

CASE 10. J. S.; age, 58; occupation, farmer; June 20, 1914. He presents himself with a large excavated ulcer of the base of the tongue extending forward along the right side of the tongue and across the back of the tongue to the left side. The tongue is badly swollen; saliva is excessive; great difficulty in masticating, and it is almost impossible to swallow food or saliva. The whole tongue is exceedingly painful. The submaxillary and cervical glands of the right side are swollen and tender. He has lost about 40 pounds in the past five weeks; is unable to sleep from the pain; cannot take nourishment except in very small quantities, and is practically unable to swallow or breathe with comfort, lying down. His whole condition is pitiable. The tissue taken from the ulcerated edges of the sore by pathologists in his home town has been reported as epithelioma. One hundred and one milligrams of radium in four separate tubes with two mm. of lead screen applied well back on the right side of the tongue and covering part of the ulceration, for 10 hours; 5 mg. of radium also applied over submaxillary glands and changed from time to time. At the end of 24 hours the patient was discharged to go home to the country with the request to return in September. On August 25, the patient returned for observation. The ulceration at the back of the tongue had cicatrized; the swelling of the glands had disappeared; enlarged glands could no longer be made out in neck; the patient had increased 20 pounds in weight and was able to masticate and swallow any kind of food; extra secretion of saliva had ceased. Patient considered himself cured. Curiously enough he had a radium burn on the tip of the right side of the tongue, which he said was very much better than a few weeks ago and was evidently healing. In all he had 1,908 mg. hours of treatment.

CASE 11. Miss A.; age, 32; occupation, clerk. Entire breast and axillary contents removed on February 15, 1914. Reported as adenocarcinoma. October 20, small nodules which had appeared in scar removed. November 21, several new, small indurations have appeared in the scar and around it. The largest is the size of an almond. Thirty-five milligrams of radium were applied to the most prominent lumps for 12 hours. December 22, marked radium burn over site of larger tumor, which is nearly gone. The smaller one has disappeared, but a number of new small nodules, the size of rice seeds, are present. One hundred and one milligrams of radium applied for 22 hours.

These cases, although few in number, represent a variety of malignant tumors, all of which are susceptible of removal by use of radium. They do not by any manner of means represent the large number of patients afflicted with cancer of various stages and conditions where the degree of the disease and complications are such that our present knowledge and experience do not

permit us to encourage them to hope for a cure by means of operative procedures, the use of radium, sera, vaccines, or any other known anticancerous therapy. None of the above-reported cases are claimed to be cures. Time enough has not elapsed for such a claim, but as we learn more of the action of radium it is believed that more of the cancer cases which are looked upon as hopeless at present may be relieved by radium alone or by a proper collaboration of radium with the various other remedies at our disposal. In spite of the great advance recently in the methods and technique in using radium, there is still much to be learned. The amount needed depends upon the different purposes of application, the different depths of tissue to be affected, the variety of tissue, the degree of malignancy, its stage, the length of time of application, and many other factors still to be settled. All these indications can be defined only after much experimentation, long continued, together with a proper appreciation of our rapidly accumulating pathological knowledge of the action of this powerful remedy on living tissues.

Many phases are developed during the course of radium treatment. Certain cases of malignant growths yield rapidly to small quantities of the remedy; on the other hand, others are stimulated apparently by small doses. Some skins are extremely sensitive to very small quantities of radium. Other patients have skin which is not affected at all by large quantities continuously applied and frequently repeated, without regard to the protection supposed to be given by screening.

Curiously, exactly similar cases of malignant growths rayed exactly the same way, with the same amount of screening, the same length of time of application, in persons of as near as possible the same age and period of time of tumor, and where the previous operative treatment was similar, may and do give exactly opposite results. For example, Cases 3 and 11 were precisely similar to another case not reported here, where the recurrent nodules persisted and increased in spite of similar treatment in every way. The pathological report was the same; recurrence took place in the same manner, but after one 15-hour application of 100 mg. she went from bad to worse and died in a few weeks. My feeling is that one application was not sufficient and that in spite of apparent failure the treatment should have been persisted in.

To the lay mind a very serious complication is the burn which sometimes follows the application. This may be extensive and deep and at times very painful and difficult of cure.

Some of my patients have noticed the more rapid disappearance of portions of the growth under the burned area than under that portion unaffected in this manner. These patients sometimes ask to have the radium left on long enough to produce an eschar, believing this to hasten the cure.

The closer the radium to the object the greater the effect of the rays. As the rays shoot out in every direction from the center the ideal course of treatment would be to have the radium as nearly as possible in the middle of the tumor. Therefore a malignant growth in one of the normal tubes of the body and within reach of radium application—as, for instance, in the oesophagus, or the rectum—is theoretically much more susceptible to treatment, especially if the malignant growth surrounds the canal than where the neoplasm can be radiated from one surface only. If there is a sinus running to or through the tumor, or if it is in a location where it can be pierced to accommodate the insertion of the radium, satisfactory treatment can also be carried on. When neither of these methods is possible, we have to resort to what is called cross-raying or cross-firing. In this means of treatment we divide the radium into capsules and place it on the opposite sides of the growth, protecting the skin from the burning rays as much as possible by means of screens of different thickness. All these details are matters of technique and depend upon the individual patient and the disease as well as upon the experience of the operator and upon his personal equation.

So little is yet known of the action of radium on living tissues and so much is still to be learned that, working as hard as one can and despite the vast amount of material, even with an ample quantity of radium, it may still be years before a proper and successful method of treatment applicable to each individual tumor can be satisfactorily and efficiently worked out.

Here are twelve patients with new growths, pathologically and clinically malignant. These neoplasms have disappeared during radium application. Following their destruction or removal the tissue at the former site of these tumors is now normal and remains so. Certainly these results merit our further careful consideration.

Radium and Roentgen Ray Therapy in Malignancy: Indications, Limitations and Recent Developments

ARTHUR U. DESJARDINS, M. D.

Section on Radium and Roentgen Ray Therapy, Mayo Clinic
Rochester, Minnesota

REPRINTED FROM

Radium and Roentgen Ray Therapy in Malignancy: Indications, Contra-Indications, Limitations and Recent Developments*

ARTHUR U. DESJARDINS, M. D.

Section on Radium and Roentgen Ray Therapy, Mayo Clinic
Rochester, Minn.

THE use of radium and roentgen rays in the treatment of certain diseases is gradually assuming a more and more important place in medicine. This is particularly true of malignant conditions, in the treatment of which radiation bids fair to become increasingly important. Unfortunately the proper evaluation of these agents, as in the case of all other therapeutic agents in their early days, is being made more or less difficult by the usual troubles of youth and by more or less exaggerated claims. All of this brings forth, from the less interested members of our profession, indications of a skepticism which, even if at times partly unwarranted, is bound in the long run to help us maintain a more judicious and more sanely critical attitude toward our work.

If we wish our progress to be steady and as free as possible from the mistakes and reversals which have marked the development of every branch of science, we must base our practice on sound principles and formulate our technique from information laboriously and patiently obtained by the physicist, the biologist, and the pathologist.

Before considering more in detail the use of radium and roentgen rays in the treatment of malignancy, I should like to emphasize briefly certain well known fundamental factors, the importance of which is not always sufficiently realized. Some of these factors impose on us limitations that we are constantly striving to overcome.

INVERSE SQUARE LAW

As we know, therapy by radiation is absolutely dominated by the inverse square law, the practical importance of which is so great that in making any application of radium or roentgen rays, it should automatically become the radiologist's first consideration.

For example, if a tube of radium is placed with relation to a malignant growth the intensity at points 0.5, 1.0, 5, and 10 cm. from the tube will be, respectively, 1, $1/4$, $1/100$, $1/400$ (taking as a unit the intensity at 0.5 cm.). If the dosage was correct for a distance of 5.0 cm. from the tube, it must follow that the portion at 0.5 cm. will be burned by a dose one hundred

times too great, while the portion at 10 cm. distance will receive little or no therapeutic effect. In principle, this law applies to both radium and roentgen rays. While this difficulty cannot be overcome completely, its consequences can be avoided to a considerable extent, as far as roentgen rays are concerned, by increasing the distance between the tumor and the source of radiation. We can thus minimize the difference between the intensity of the rays as they enter the proximal surface of the tumor and as they leave the distal surface. In other words, the different parts of the tumor will receive a more uniform quality of radiation. However, the associated disadvantage is a great loss in the total intensity available, a loss which must be compensated by a great increase in the time of exposure.

Another way of avoiding the consequences of the inverse square law is to increase the number of sources of radiation; this may be accomplished by multiplying the number of areas treated. In this way, as many multiples of a single dose may be concentrated into a limited internal area as the number of different superficial areas through which the treatment can be given. This latter method should be selected in treating a tumor situated at approximately equal distances from two opposite surfaces of the body. In some cases a combination of the two methods may be advisable or necessary. However, should the tumor be superficial, increase in focal distance alone is to be preferred as a means of increasing the dosage delivered to the tumor. Such increase in distance should, of course, be adequately compensated by increase in time of exposure.

The only way to overcome the handicap of the inverse square law with any degree of effectiveness in the case of radium is by burying the radiation units in the tissues and increasing the number of those units. This may be accomplished by inserting into the tissue tubes of radium or its emanation which are allowed to remain in place either temporarily or permanently. However, because of the short and rapidly decreasing period of activity of radium emanation, and because of the necessity of leaving in place the small glass containers, but particularly because of the

intense necrosis produced around such unfiltered radiation elements, the use of buried emanation, while undoubtedly of great value in many cases, will probably be gradually replaced, at least to some extent, by the use of radium needles containing a definite quantity of radium salt of stable activity. These needles, with varying degrees and qualities of filtration, aid in avoiding some of the tissue necrosis occurring around an unfiltered glass emanation unit. Such necrosis is definite and complete within a zone, the extent of which is proportionate to the radium content of the tube. ⁽²⁾

The question of filtration is becoming more and more important. We know that the rays from a roentgen ray tube or from a radio-active substance, such as radium or its emanation products, are not homogeneous, that is, they are not made up of rays of one wavelength. On the contrary, such rays are extremely heterogeneous, being composed of a mixture of rays of all wavelengths. The longer, being easily absorbed or weak in penetrating power, do not pass beyond the first layers of tissue cells, while the rays of shorter wave-lengths penetrate deeper and deeper into the tissues. This complex character of roentgen rays and radium rays, to which their unequal absorptibility is due, constitutes another major limitation in efficient therapy by radiation, a limitation almost as great in its effects as the inverse square law. Such limitation may be minimized to a considerable degree by filtration. In treating a malignant tumor with roentgen rays, attack must generally be made through the skin or mucous membrane, both of which are extremely sensitive to so-called soft rays, or rays of long wave-length. This fact has brought grief to many radiologists in the past, and we still occasionally are reminded that the skin will withstand only a limited degree of insult. By adequate filtration, wave-lengths least injurious to the tegument can be selected. In other words, the softer rays are absorbed by the filter which prevents them from injuring the skin or mucous membrane. Another very important point is accomplished, namely, an increase in the homogeneity of the effective radiation, or rather a decrease in its heterogeneity.

*—Presented before the Radiological Society of North America, December 7-9, 1921, Chicago.

The situation with regard to radium is quite different. If we wish to treat a lesion by external application we must use heavy primary and secondary filtration in order to avoid serious burns. One millimeter of platinum or its equivalent will filter out all the β rays and the less penetrating portion of the γ rays. Two or three millimeters of rubber will eliminate the secondary rays generated by the primary radiation in the metal used as a filter. If we wish to attack a lesion by burying in it radium or its emanation, filtration may not be necessary, especially in tumors of relatively small size. Around each unit of radium or its emanation so placed, there occurs destruction in the form of necrosis which may be more or less extensive according to the dosage. Beyond this zone of necrosis, the tissue constituents of which act as a filter, a so-called selective effect is obtained. The tissue adjoining the radio-active substance filters out the softer, less penetrating rays, to which the necrotic effect is due, and the effect of that portion of the radiation which has gone through this zone unabsorbed then depends on the radio-sensitiveness of the tissue cells outside that zone. When buried emanation is used the zone of destruction is greater because nearly all of the β and γ radiation passes out of the glass tube; whereas with platinum needles, or other filters of relatively high density which allow the escape of only the more penetrating portion of the β and γ radiation, the zone of destruction is more limited.

By far the most serious limitation in the diagnosis and treatment of pathologic lesions springs from the fact that we must depend almost entirely on our human eyes and hands. These are very gross instruments and, even with very effective therapeutic agents, we can never hope to accomplish the cure of more than a certain proportion of the malignant diseases we may undertake to treat. Those of us who have had experience with pathologic conditions found at necropsy know but too well the uncertainties and deceptions of our methods of physical diagnosis. Some consolation may be derived from the fact that the radiologist's limitations in this respect are shared equally by the surgeon and the internist. It is a very common occurrence to find that a malignant lesion supposedly limited to a certain organ or tissue had actually become much more widely disseminated either by direct extension, by metastasis, or by both. The only way we have of combating this limitation is by impressing on the public and members of the profession in general the extreme importance of early diagnosis and treat-

ment. Although something can be accomplished in this direction, the very limitation in the acuity of our senses often makes an early diagnosis in the first instance difficult. It is not unusual to be told by patients that when they first consulted a physician concerning a lesion which appears to have been an early manifestation of a malignant process they were told that it was of no significance and that they should promptly forget it. Such instances influence us to conclude that physicians are as much in need of "education" as the public in this most important matter.

INDICATIONS AND CONTRA-INDICATIONS FOR RADIUM AND ROENTGEN RAY THERAPY

Our first consideration must be the diagnosis, because, if we are to utilize radium or roentgen ray therapy with any degree of success, we must know the nature of the lesion we wish to treat. Not only should we know the type of malignancy, but as many as possible of its salient features, such as the predominating type of cell, and reaction factors. It is not always possible, nor in some cases is it necessarily advisable, to obtain such complete information. Judgment should be applied to the individual case. The lack of a definite diagnosis constitutes a fundamental contra-indication to such treatment. The other important contra-indications are:

1. The bad general condition of the patient, making it impossible or dangerous to administer really adequate treatment.

2. Tumors complicated by infection. This condition is not infrequently encountered, especially in association with carcinoma of the uterus, but occasionally also in other locations such as the breast. In such cases drainage and other general measures must be instituted before radiation.

3. Lack of suitable apparatus, or the knowledge requisite for its proper use. We occasionally still hear of physicians attempting to treat malignant conditions with such facilities as are provided by an ordinary portable bed-side unit.

Radium is particularly indicated when we are dealing with a fairly small lesion or tumor at or near the surface of the body (or reasonably accessible from the outside) and the extent of which can be outlined with a fair degree of accuracy. Its ideal indication is in conditions in which it is possible to introduce the agent into the substance of the lesion in such a manner as to deliver to every part fairly uniform radiation in adequate dosage.

At the present time radium, alone or in conjunction with roentgen rays, is indicated and should be used (preferably by the needling method) in cases of solitary glandular carcinoma or sarcoma of limited size and well defined extent, especially on or near the surface of the body and in cases of solitary or discrete, superficial, malignant gland or cutaneous metastasis. Malignant conditions in cavities accessible from the body surface (uterus, vagina, rectum, bladder, mouth, nose, larynx and esophagus) should preferably be treated with radium or its emanation, usually in conjunction with external roentgenization. In cancer of the uterine cervix, for instance, radium achieves marvelous results in many cases because the element can be introduced into the cervical canal and is there surrounded on all sides by the neoplastic tissue. From our present knowledge the method of employing therapy by radiation to the best advantage in such conditions would seem to lie unquestionably in the combination of radium internally and roentgen rays externally.

The γ rays of radium are more penetrating than the roentgen rays used at present for therapeutic purposes. Experimentally, roentgen rays have been produced with wave-lengths as short as some of the γ rays, and these may be available before long. However, with the small dosages commonly used, the total radio-active energy delivered to a lesion or tissue beneath the surface is very small, and constitutes an extremely small fraction of the total radiation generated by a given quantity of radium. Furthermore, our present means of employing radium for therapeutic purposes are such as to make it impossible to deliver uniform radiation to a lesion of any extent on the surface. This difficulty is magnified many times when we are dealing with a deep lesion the exact extent of which cannot be outlined accurately. These factors determine in a very large measure the indications for the use of radium or roentgen rays.

Roentgen rays act at a more uniform intensity over a much wider field than radium rays. Although their intensity decreases rapidly as they pass from the surface to deeper and deeper tissue layers, a portion of this loss can be compensated by increasing filtration, focal distance, and the number of so-called ports of entry. Therefore, if we are dealing with an extensive superficial lesion or with a lesion, either superficial or deep, whose exact extent cannot be fairly accurately outlined, roentgen rays are the agent of choice. Tumors with a tendency to metastatic dissemination by way of the lymphatics,

or growths in which metastasis is suspected or to be expected, should be treated either by roentgen rays alone or combined with radium. The neck with its complicated lymphatic system in malignancy of the mouth or face, and the thorax and axilla in cancer of the breast serve as illustrations.

Combination of roentgen rays and radium.—Although the indications for roentgen rays or radium are usually quite well defined, there are many cases in which both should be used in conjunction. As a matter of fact, the ideal method of treating many malignant tumors is by a judicious selection or combination of surgery, roentgen rays, and radium. In selected cases, surgery should be a preliminary step to prepare the field and to permit direct visual application of the radium, to be supplemented or not by roentgen radiation. If anything really substantial is to be accomplished in the therapy of malignant conditions by radiation, our procedure must be based on one essential requirement. The entire involved area with its lymphatic drainage, must receive a uniform lethal dose, which should be delivered, as nearly as possible, during the first treatment. I do not mean to imply that it is necessary to give such dosage at one seance, but the treatment should be completed within as short a period as the condition of the patient and the degree of reaction will allow. To scatter a course of treatment over a period of weeks is to defeat the very purpose we are attempting to achieve. If involvement is limited and it is reasonable to expect a cure, we should aim to destroy the malignant elements by one attack. As heavy dosage as the integrity of important neighboring structures will allow should be administered with adequate filtration in order to minimize as much as possible the deleterious effects of the long wave-length portion of the radiation. Limited radiation with limited dosage is to be used when a cure is out of the question and only palliation is to be expected.

The importance of treating the lymphatic system draining the area of a malignant tumor cannot be overemphasized. Untreated elements not uncommonly show signs of activity. This is of especial importance in carcinoma, the dissemination of which takes place so largely by way of the lymphatic system. Although this consideration might seem self-evident the manifest lesions only are often treated in a scattered fashion and the lymphatic drainage system overlooked. In fact, in most malignant conditions the lymphatic drainage system should be treated before attacking the main lesion. In gen-

eral, we should adopt the same procedure in sarcoma, although in these cases dissemination by way of the blood stream is the rule. The anatomy and physiology of the circulatory system and the general pathologic features of carcinoma and sarcoma enable us to understand why in the former metastasis usually takes place through the lymphatic system but in the latter occurs by way of the blood stream.

Sarcoma, especially sarcoma of bone, has a very great tendency to metastasize to the lungs. ⁽¹⁾ It is difficult to say why this is true. There seems to be very little doubt that the dissemination of metastatic elements or emboli takes place quite early and the reason many of these do not lead to gross secondary lesions possibly is due to the activity of some defensive mechanism elaborated in the body fluids as the result of the antigenic action of the primary growth. An explanation of the fact that metastatic elements which give rise to secondary lesions have such a predilection for the pulmonary organs may perhaps be found in the fact that the pulmonary circulation constitutes the first capillary bed through which the blood from the general circulation passes.

Whatever may be the truth with regard to metastasis, the questions arise: Should we make it a routine practice to radiate the mediastinum and lungs in sarcoma in the hope of destroying metastatic deposits, even if not demonstrable? Should we radiate the mediastinum and lungs at all? Should we treat only these organs or should we attempt to radiate the entire trunk on the basis that, while pulmonary metastasis is the most frequent site, metastasis not infrequently occurs in other organs?

In a recent personal communication, Bloodgood writes with regard to this question: "In a number of cases the x-ray (examination) of the lungs was negative, and after amputation, radiation of the chest was performed on one or more occasions; in spite of which metastasis developed. Similar observations in three cases of sarcoma of the soft parts. Up to the present time I have no evidence that radiation of metastasis of the lungs has had any effect even if done before metastasis shows in the x-ray." From this statement we are forced to accept one of the three following conclusions: (1) the dosage was inadequate, (2) the quality of the radiation was not suitable, or (3) radiation will not achieve the destruction of such metastatic foci. There is the further possibility that if radiation is to be really effective in controlling metastatic dissemination to the

lungs not only the mediastinum should be treated, but also the lungs, because metastatic emboli must often be carried beyond the larger radicles well into the substance of the organ.

If an attempt is made to administer so-called prophylactic treatment to the contents of the thoracic cavity for metastatic sarcoma or carcinoma, such treatment should be extremely thorough and should be given early, even though it be impossible to demonstrate metastatic foci.

Unfortunately, in the majority of cases when the liver or lungs become demonstrably involved, the condition is usually almost hopeless. We may, however, look forward to the time when further developments in technique may make it possible to do more toward checking metastatic deposits. Pfahler has shown that in some cases it is possible to influence the development of metastasis in the bony substance of the vertebral segments. However, we are not justified in increasing the discomfort and suffering of a dying fellow-being when we know that all our previous efforts to cure him have been unsuccessful.

The group of malignant conditions classified under the general head of lymphoblastoma, which includes Hodgkin's disease, lymphosarcoma, and allied conditions, presents a difficult problem. Characterized as these are by a tendency to progressive involvement of the lymphatic elements their exact status remains unsettled. In many cases in which the cervical glands are enormously enlarged, we can obtain a rapid and at times a truly startling reduction by means of radium. Other important groups of glands such as the mediastinal, and paravertebral, should also be treated, and this can be done most efficaciously by roentgen rays. It is questionable if the reduction of enormous adenopathies by radium may not in some cases be too rapid, and if a more gradual, though slower, regression would not yield better results. For the present we must be guided by our judgment in individual cases.

Preoperative radiation.—The practice of radiating a region after preliminary surgical amputation of the grossly malignant tissue has become a routine practice in many cases as in carcinoma of the breast. Although a sound technique may yield good results, it is doubtful if our hopes are really justified or will be realized. Often operation performed with the intent to rid the patient of cancer leads to more or less rapid dissemination by grafting, or by venous or lymphatic absorption. The rational procedure, therefore, would seem to be for the surgeon not to op-

erate before the involved part and its lymphatic drainage have been thoroughly radiated. Aside from the principle involved this would be of decided advantage in cases of carcinoma of the breast particularly, because the radiation could be administered much more effectively before operation, since there would not be a recent wound to prevent the arm from being well abducted. The entire axilla could thus be much more thoroughly and uniformly treated, and the tendency to malignant cell dissemination at the time of operation would be diminished. This principle may be applied to the surgical treatment of malignant conditions in general, except, of course, in the cases in which surgery is intended as a preliminary step before radiation.

The surgeon wishes to know how long an interval should be allowed between radiation and operation. The early response of tissues subjected to radiation consists essentially in a modified inflammatory reaction, beginning as usual with edema; the reaction is more intense and more localized, if radium is used, and less intense and more diffused if roentgen rays are used. The tissue cells gradually recover if the dose has been light; there is inhibition of their reproduction and development if the dose has been moderate; the cells are completely destroyed if the dose has been lethal. The products of such destruction are removed by autolysis and absorption, and later are replaced by fibrosis. This is true of normal as well as of pathologic cells. Generally neoplastic cells are more sensitive to radiation than normal tissue cells, and on this fact is based the entire radiation treatment of malignancy.

In many patients radiation produces so-called deep radiation sickness, a temporary state characterized by nausea with or without vomiting which may be quite pronounced, anorexia, headache, a sensation of general weakness, and nervousness and sometimes by fever. This state may last in some degree for from a few hours to several days; a few patients remain nauseated and weak for as long as two weeks, during which time they eat little and lose weight. Such reaction, which is usually shorter and much less severe in persons treated with radium than in those treated with roentgen rays should be allowed to subside completely before the patient is subjected to the ordeal of a major operation.

As a rule, severe reactions are observed only when some part of the abdomen has been treated, and this is particularly true of the upper half. Therefore, the interval between radiation and operation must depend largely

of the relative importance of these factors in a given case. In carcinoma of the breast radiation sickness is usually either absent or slight and so the operation could readily follow within a week. In carcinoma of the uterus, however, the radiation is administered by means of radium internally and by external roentgenization, and the interval should be from three to four weeks.

After radiation the tissues should be in comparatively good condition for operation, and the surgeon should not encounter any particular delay in the repair of the wound. It is doubtful if the surgeon will have any difficulties in carrying out the various steps of the operation, after a single course of treatment, especially if a proper interval has been allowed before operation. Even though the operation is made more difficult by radiation, few surgeons would hesitate to adopt it if the final results from the standpoint of the patient can be improved. Preoperative radiation should also tend to minimize the danger of tampering with a malignant lesion in order to obtain a specimen for diagnosis.

Postoperative radiation.—Postoperative radiation may be and often is more or less illusory. The most important requirements in rendering innocuous such invisible malignant elements as may have remained after surgical ablation is a correct selection of the agent and its use in adequate dosage. Should radium or roentgen rays be used? If we wish to sterilize an entire region, as following removal of the breast, radiation should be administered not only to the field of operation, but to its lymphatic drainage. Roentgen rays properly applied will best meet the condition. Radium should be reserved for small well-defined territories, especially if the agent can be introduced into the center or the substance of the tissues, as the vaginal vault following hysterectomy (in conjunction with roentgen rays from the outside), or into the cavity left after the removal of a tumor of limited size. However, in the latter, the radium should preferably be introduced at the time of and as a part of the operation. Radium used postoperatively, and blindly pushed or slipped into a drainage tube placed by the surgeon at the time of the operation is, at best, a very uncertain procedure.

If there has been no preoperative radiation, the patient should receive the treatment as soon as possible after operation. If the operation has been preceded by radiation the postoperative interval must be governed by the preoperative interval; due consideration should be allowed between operation and radiation. In cases of carcinoma

of the breast treatment might be commenced within one week, whereas it might seriously jeopardize the patient's chances of recovery if radiation were begun so soon after an abdominal operation.

How often should this postoperative, or so-called prophylactic radiation be repeated? In the absence of glandular involvement if the dosage has been estimated correctly, two to three thorough courses of treatment should be sufficient, particularly if one of these courses has been administered before operation. If the dosage has not been correctly estimated, however, we can hardly expect to achieve good results by prolonging our efforts indefinitely.

RECENT DEVELOPMENTS IN TECHNIQUE

During the past few years radiologists and members of the medical profession in general have been startled out of their usual complacency by reports of wonderful advances in the roentgen ray therapy of malignant diseases. Such reports have emanated very largely from German clinics and have led us to believe that very much better results can be obtained than formerly.

A study of original sources and the reports of several American observers in Germany show that no two of those clinics employ the same technique. Although there is a wide difference of opinion with regard to many details in the application of treatment, there is a reasonable degree of unanimity on a few points: (1) the use of higher voltage; (2) the use of "higher" filtration and the advantages of copper or zinc over aluminium as a filter; and (3) the use of increased focal distance. There are strong theoretical reasons for believing that these factors will exert a great influence on pathologic processes of a neoplastic nature, but only time and greater experience will enable us to decide whether or not such influence will be purely beneficial and to what extent.

Seitz and Wintz⁽⁵⁾ have advanced the idea, based on what seems to be very painstaking research, that different malignant and other conditions respond to definite dosages. Thus, they have found that the dose for carcinoma lies between one hundred and one hundred and ten per cent of the unit skin dose; the dose for sarcoma is given as from sixty-five to seventy per cent, and the dose for castration was determined to be thirty-five per cent. These figures, I believe, were not intended to be interpreted too literally. It would be very difficult indeed to reconcile any such fixed limits of dosage with what we know of the very considerable variability in the metabolism of a given type

of malignant cells. For example, in carcinoma there is often a tremendous difference in activity between tumors in patients of the same age, not to mention the variable activity of tumors in patients of different ages. Even the influence on the growth of tumors of such factors as lymphocytic infiltration, fibrosis, differentiation, and hyalinization, either singly or in combination⁽³⁾, make it very difficult to accept such arbitrary ideas of dosage.

BIBLIOGRAPHY

- 1—Bloodgood, J. C.: The Diagnosis and Treatment of Benign and Malignant Tumors of Bone. *J. Radiol.* 1920: 1, 147-238.
- 2—Lacassagne, A.: Recherches Experimentales sur L'Action des Rayonnements β et γ et du Radium agissant dans les Tissus par Radiopuncture. *J. de Radiol. et d'Electrol.*, 1921: 5, 160-173.
- 3—McCarty, W. C.: Factors Influ-

encing Longevity in Cancer. In press.

- 4—Pfahler, G. E.: The Treatment of Metastatic Carcinoma of the Spine by Deep Roentgen Therapy. *Jour. Roentgenol.*, 1919, ii 326; *Surg. Gynec. Obst.* 236, Sept., 1919.
- 5—Seitz, L. and Wintz, H.: Methode der Roentgen-therapie und ihre Erfolge. Urban and Schwarzenberg, 1920, 423 pp.

