THE ACTION OF RADIUM ON CANCERS OF THE PELVIC ORGANS

A CLINICAL AND HISTOLOGIC STUDY *

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Since April, 1914, I have treated 112 cases of malignant growths of various regions of the body with radium. Forty-eight of these occurred in pelvic organs. Forty-one of these pelvic cancers are considered in this paper. Thirty-six were in the uterus, five in the rectum and three in the bladder. The tumors were inoperable, recurrent or operable carcinomas. Twenty-four were inoperable, nine recurrent and eight operable.

Ten of the inoperable and three of the recurrent carcinomas were thoroughly cauterized or excoriated and then cauterized preceding the application of radium. Broken-down tissue and debris were thereby as completely removed as possible, and the extent of the intensity of the gamma rays into the depths of the tissues correspondingly increased. The operable cases were subjected to an extensive vaginal cauterization and an abdominal panhysterectomy. As soon as the patient recovered from the operation, radium was inserted into the crater of the broad ligament. The rays were used as a prophylactic to recurrence.

I wish to draw attention to the remarkable deodorizing and purifying action of radium. Those who have attended patients after such abdominal panhysterectomies well remember the sloughing of tissues in the crater of the broad ligament, which gives rise to a

cauterizations always were performed with ordinary soldering irons at red heat.

THE TECHNIC

The technic of applying the radium varied as to the limiting of time of the applications and the kind of metal filters used, but not in the amount of milligrams of radium element applied (uniformly 50 mg.).

Fig. 2 (Case 33).—High power magnification of Area *d* in Figure 1: *a*, carcinoma cells; *b*, connective tissue.

Fig. 1 (Case 33).—Carcinoma, portio vaginalis, cervix uteri. Low power reproduction of tissue removed Feb. 6, 1915, at beginning of treatment: *a*, squamous cell carcinoma; *b*, connective tissue; *c*, lymphocytic infiltration; *d*, area reproduced in Figure 2.

terrific putrid odor and discharge and an irregular temperature. One, or at the most two applications of radium stop these distressing complications. The

In the beginning of my radium work, the duration of each application was from ten to twelve hours, occasionally twenty-four hours. The interval between the treatments varied from seventy-two to ninety-six hours. These applications were continued until a decided improvement occurred in the subjective as well as the objective condition of the patient. This usually took place after a dosage of from 3,000 to 4,000 milligram hours had been reached. The treatments were then given weekly and finally biweekly, until the condition of the patient warranted a cessation of the treatments. Frequent examinations were insisted on to keep the patient under control. A total dosage of from 8,000 to 10,000 or more milligram hours was thus recorded.

Fourteen patients were treated in this manner (Cases 2, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18). A subjective improvement was usually noticed after the third application. The pain decreased, the profuse purulent, creamy discharge became scanty and serous, and the hemorrhage ceased. The general state of health improved correspondingly. After about 3,000 milligram hours of radium element had been given (that is, after from about twenty-one to twenty-four days, the bimanual findings became usually normal. In a few cases such a state was not reached until about 6,000 milligram hours had been applied. The uteri which were firmly fixed at the first examination became freely movable and could be plainly outlined. The adnexa were palpable and the crater in the cervix was covered with healthy granulations, being protected by a grayish or whitish membrane. The parametria also were free of any indurating bands. In other words, by cautious procedures and careful obser-

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vation, we established the fact that on an average from 3,000 to 4,000 milligram hours of radium element were necessary to attain an apparently objective cure.

This knowledge led to the second mode of treatment, which I may term the "intensive method." Just as maximum dosage of Roentgen rays may be concen-

occur in this method, they were very mild and of very short duration, lasting usually a day or two.

3. Destruction, ulceration or necrosis of the tissues was of regular occurrence. Repair of these defects was slow. Fistula formation, vesicovaginal, recto-

Fig. 3 (Case 33).—High power magnification of tissue removed Feb. 18, 1915, after 2,400 milligram hours of radium element had been applied from Feb. 6 to 8, 1915: *a*, enlarged carcinoma cells; *b*, lymphocytic infiltration; *c*, note connective tissue fibers surrounding groups of carcinoma cells.

Fig. 4 (Case 33).—Low power magnification of a section of tissue removed Feb. 28, 1915, after 4,800 milligram hours of radium element had been applied from Feb. 6 to 8 and Feb. 18 to 20, 1915: *a*, carcinoma cells; *b*, connective tissue cells; *c*, area reproduced in Figure 5 under high power.

trated into the possibly shortest space of time, so the milligrammage of radium element might be given within the shortest limit of time, and from 3,000 to 4,000 milligram hours of radium element were applied within from sixty to eighty consecutive hours.

Ten cases in particular (Cases 1, 3, 4, 14, 20, 23, 25, 26, 27 and 28) were thus treated. Although we obtained the same primary results as with the first method, we, however, noted the following points:

1. The apparently objective cure was not reached any sooner than with the first method.

2. The associated symptoms were exceedingly stormy and much severer. They consisted, chiefly, in a marked loss of weight, strength and appetite, with hyperpyrexia, obstinate vomiting, profuse diarrheal stools and obstinate dysuria. Although these symptoms were only transitory, lasting from eight to ten days, the patient suffered much, a condition which we rarely observed in the cases treated by the first or "intermittent method." If such manifestations did

Fig. 5 (Case 33).—High power magnification of area marked *c* in Figure 4: *a*, area of necrobiotic tissue; *b*, area of connective tissue; *c*, cytolytic carcinoma cell.

vaginal or even intestinovaginal, occurred in ten cases. However, I wish to state that fistula formation existing at the time of the beginning or taking place during the first few days of the course of the treatment must be ascribed to the extensive cauterization. The damaging action of the radium rays is a contributing cause (Cases 1, 4, 6, 15, 20, 26, 29 and 46), while fistula formation occurring from three to four weeks after the beginning of the radium applications must be directly attributable to the destructive action of radium, and extensive invasion of the bladder or bowel with cancer forms the predisposing cause (Cases 2, 8 and 33).

Finally, the following plan of treatment was adopted and carried out in the rest of the cases:

A course consists of from six to eight séances of from ten to twelve hours each, with an interval of from thirty-six to sixty hours. This course is followed by an intermission of three weeks. If a bimanual examination made at this time reveals an apparent cure, two or

three applications of from 500 to 600 milligram hours of radium element are given every second or third day. Another interval of three weeks is allowed, and if the examination then reveals a normal condition, the treatment is considered terminated. Negative findings, of course, are followed by another course of from 3,000

walls were protected by snugly packing the vaginal canal with gauze, Para rubber or lead plates surrounded by rubber and gauze.

CLINICAL RESULTS

Tables 2 to 5 show at a glance the results of the

Fig. 6 (Case 39).—High power reproduction of cervical tissue removed March 16, 1915: *a*, nest of carcinoma cells; *b*, karyolysis of nuclei; *c*, granulation of protoplasm; *d*, vacuolation of protoplasm; *e*, connective tissue.

Fig. 7 (Case 39).—High power magnification of tissue removed from center of cervix, March 28, 1915, after 1,600 milligram hours of radium element had been applied from March 20 to 26, 1915: *a*, degeneration of nuclei; *b*, granulation of protoplasm; *c*, degenerating carcinoma cell; *d*, mitosis of cell; *e*, lymphocytes.

to 4,000 milligram hours. This "interval method" gave the best subjective and objective results with a minimum of concomitant symptoms, so that I consider it the method of choice.

Lead filters of 1, 2 and 3 mm. thickness were used in my first work. A 1 mm. filter was deemed sufficient for intra-uterine applications, while the heavier filters were employed in vaginal, rectal and vesical cases. Following the advice of Adler, Werner and others, I soon replaced the lead with brass filters of from 1 to 1.5 mm. thickness. Whether or not the lead filters cause severer latent destructions of tissue than brass filters I am unable to prove. Such disturbances occurred either in very advanced cases of carcinoma, with breaking down uterine or vaginal walls, or in extensively cauterized tumors, as mentioned before. The secondary rays produced in the metal filters were arrested by surrounding the filter with a cot made of pure Para rubber of a thickness of from 1 to 3 mm. The healthy vaginal

Fig. 8 (Case 39).—High power magnification of tissue removed April 7, 1915, after 3,700 milligram hours of radium element had been applied from March 26 to April 4, 1914: *a*, macrophagia-connective tissue cells; *b*, connective tissue cells; *c*, necrobiotic carcinoma cell; *d*, vacuolation of protoplasm.

radium treatment. The amount of the milligram hours of radium element used, and beginning and duration of the treatment and the present condition are enumerated for each case. Of the ten cases of Table 2, one case was refractory, and nine cases evidenced a subjective and an objective improvement. Objective improvement indicates negative findings on bimanual palpation. Five of this group have succumbed to the disease. One has remained well since April, 1914, one since October, 1914, and one since January, 1915. Two cases, 39 and 40, are of too recent date to permit an expression as to the remote results. The primary results in these cases, however, are very good. Three of these patients (Cases 12, 16 and 18) were subsequently

subjected to an abdominal panhysterectomy.

Fourteen inoperable cases, enumerated in Table 3, were treated only with radium. They were far advanced or extremely cachectic cases or had constitutional manifestations contraindicating even a cauter-

ization. Ten have died or are slowly succumbing to the disease. Four are free of all objective and subjective symptoms. They, and three cases not yet listed, were treated only recently; and considering the poor results obtained in the other ten cases, I must withhold a final opinion. One case (Case 14) had, after the completion of radium treatment, a panhysterectomy.

Of the nine recurrent carcinomas, listed in Table 4, five show an entirely refractory behavior toward the radium rays. Four revealed a subjective and three also an objective improvement. One of the latter patients died eight months after the beginning of the treatment from an intercurrent disease. She had had a recurrence the size of a pea, which disappeared after

TABLE 1.—CANCERS OF PELVIC ORGANS TREATED WITH RADIUM

Case No.	Name of Patients	Hospital Number	Age, Yrs.	Date of Adm.	Uterine	Rectal	Vesical	Milligram Radium Element	Operable	Recurrent	Inoperable		Remarks
											Cauterized	Not Cauterized	
1	Mrs. B.	Augustana.....	41218	51	9/24/14	+	..	4,200	+	..	..	+	Cauterization 11/3/14. Op. four years ago.
2	Mrs. H.	Augustana.....	40098	49	5/22/14	+	..	9,525	..	..	..	+	
3	Mrs. H.	Augustana.....	40717	61	7/23/14	+	..	10,350	..	+	..	..	
4	Mrs. R.	Augustana.....	40944	39	8/25/14	+	..	6,775	+	..	..	..	
5	Mrs. D.	Augustana.....	39516	32	3/23/14	..	+	9,900	..	..	..	+	Cauterization 9/16/13.
6	Mr. E.	Augustana.....	40405	74	6/29/14	..	+	3,150	+	..	..	..	
7	Mr. J.	St. Mary's.....	25176	57	6/30/14	..	+	2,175	+	..	..	..	
8	Mrs. K.	St. Mary's.....	24058	38	3/13/14	+	..	5,700	..	+	..	..	
9	Mrs. K.	Augustana.....	39778	66	4/22/14	+	..	6,320	..	..	+	..	Became operable.
10	Mrs. McQu.	Augustana.....	39516	29	3/23/14	+	..	3,375	..	+	..	..	
11	Mrs. McC.	St. Mary's.....	24096	47	3/17/14	+	..	7,500	..	..	+	..	
12	Mrs. M.	St. Mary's.....	23957	52	3/ 7/14	+	..	7,875	..	..	..	..	
13	Mrs. P.	Augustana.....	40270	63	6/11/14	+	..	2,575	..	+	..	..	Became operable. Carc. corp. uteri. Became operable. Also cauterization. Became operable.
14	Mrs. R.	Augustana.....	40202	43	6/ 4/14	+	..	9,250	..	..	..	+	
15	Mrs. C. S.	Willard Hosp.		52	4/ 4/14	+	..	8,312	..	..	..	+	
16	Mrs. Th.	Augustana.....	39321	53	3/ 4/14	+	..	9,043	..	..	..	+	
17	Mrs. V.	Augustana.....	39755	64	4/19/14	+	..	3,525	+	..	..	..	Became operable. Carc. corp. uteri. Became operable. Also cauterization. Became operable.
18	Mrs. W.	Augustana.....	39469	35	3/19/14	+	..	8,700	..	..	..	..	
19	Mrs. W.	Augustana.....	40568	48	7/14/14	+	..	3,750	..	..	..	..	
20	Mrs. P.	Augustana.....	40456	45	7/ 4/14	+	..	3,500	..	+	..	..	
21	Mrs. J.	Augustana.....	40349	26	6/22/14	..	+	1,125	..	..	..	+	Carc. corp. uteri.
22	Mrs. R.	Augustana.....	41305	32	10/ 7/14	+	..	4,000	..	..	..	..	
23	Mrs. Sk.	Augustana.....	41221	53	9/25/14	+	..	6,800	..	..	..	..	
24	Mrs. B.	Washington Bvd.	8968	52	10/17/14	+	..	4,150	+	..	..	..	
25	Miss Ro.	Washington Bvd.	8902	53	10/ 1/14	+	..	8,875	..	..	..	..	Cauterized 11/22/14. Sarcomatous myoma ?
26	Mrs. H.	Augustana.....	41612	52	11/21/14	+	..	2,300	..	+	..	..	
27	Mrs. M.	West Side.....	28985	48	11/27/14	+	..	4,150	..	..	..	..	
28	Mr. St.	St. Mary's.....	26857	52	12/29/14	..	+	3,600	..	..	..	..	
29	Mrs. T.	Augustana.....	41944	49	1/ 5/15	+	..	3,500	..	..	..	..	Colored.
30	Mr. To.	St. Mary's.....	27096	58	1/23/15	..	+	2,400	..	..	..	..	
31	Mr. A. M.	Willard.....		52	2/10/15	..	+	4,500	..	..	..	..	
32	Mrs. M.	Augustana.....	42319	42	2/15/15	..	..	5,175	..	+	..	..	
33	Mrs. H.	Post-Graduate....		43	2/ 6/15	+	..	4,800	..	..	..	..	Well. Pelvis normal
34	Mrs. H.	St. Mary's.....	27533	33	3/ 3/15	+	..	2,800	..	+	..	..	
35	Mrs. C.	St. Mary's.....	27590	52	3/ 9/15	+	..	3,900	..	+	..	..	
36	Mrs. L.	Augustana.....	42538	60	3/ 9/15	+	..	2,925	..	..	+	..	
37	Mrs. W.	Norwegian Deaconess..		63	3/ 7/15	+	..	1,700	..	..	..	+	Died August, 1914 from invasion of bladder and exhaustion. Died December, 1914 from exhaustion.
38	Mrs. J.	St. Mary's.....	27560	36	3/ 5/15	+	..	2,550	+	..	..	..	
39	Mrs. St.	St. Mary's.....	27649	65	3/15/15	+	..	3,700	..	..	..	..	
40	Mrs. DeR.	St. Mary's.....	27978	56	4/14/15	+	..	5,650	..	..	..	..	
41	Mrs. St. A.	St. Mary's.....	27982	49	4/15/15	+	..	3,950	+	..	..	..	Well except fistula.

TABLE 2.—INOPERABLE CANCERS TREATED WITH CAUTERIZATION AND RADIUM

Case Number	Cause of Inoperability	Date of Cauterization	Total Mg. Hrs. of Radium Element Applied	Duration of Treatment	Primary Results			Further Treatment	Results and Present Condition
					Refractory	Subjective Improvement	Objective Improvement		
9	Involvement of bladder and parametrium	4/23/14	6,320	5/12/14 to 7/ 5/14		Yes		None.....	Died from bladder and vulva invasion.
11	Involvement of bladder and rectum	3/18/14	1,750 3,200 2,550	4/14/14 to 4/23/14 6/17/14 to 7/23/14 8/12/14 to 8/23/14		 Yes		 None.	Died. Patient after remarkable primary result neglected to return until June. Radium now refractory. Died Dec. 20, 1914 from invasion of rectum.
12	Extensive involvement of parametrium and rectum	3/ 8/14	7,875	4/ 2/14 to 6/11/14		Yes	Yes	July 14, 1914. Abdominal panhysterectomy	Died Dec. 20, 1914 from invasion of rectum.
16	Involvement of parametrium	3/ 5/14	9,043	4/ 1/14 to 9/ 9/14		Yes	Yes	April 24, 1914. Abdominal panhysterectomy	Well. Pelvis normal
18	Marked cachexia...	3/20/14	8,700	4/ 1/14 to 7/31/14		Yes	Yes		Died August, 1914 from invasion of bladder and exhaustion. Died December, 1914 from exhaustion.
22	Extensive involvement of vaginal vault	16/ 8/14	4,000	10/17/14 to 10/22/14	Yes				Well. Pelvis normal.
23	Extensive involvement of vagina and parametrium	9/26/14	6,800 1,200	10/19/14 to 11/ 1/14 2/ 9/15 to 2/11/15		 Yes	 Yes		Well. Pelvis normal.
29	Involvement of anterior vaginal wall	1/ 6/15	3,500	1/21/14 to 1/24/15		Yes	Yes	Repair of vesico-vaginal fistula March, 1915	Well except fistula.
39	Involvement of parametrium	3/16/15	3,700 850	3/20/15 to 4/ 4/15 4/26/15		Yes	Yes		June 11, 1915; metastasis of right inguinal glands.
40	Involvement of bladder and parametrium	4/ 7/15	5,650	4/15/15 to 5/ 6/15		Yes			Panhysterectomy could not be completed. Supravaginal amputation.
36	Pyometra; involvement of parametrium	3/10/15	2,925	3/12/15 to 3/23/15		Yes	Yes		

radium treatment and cauterization. Another patient after a successful primary result did not return for a reexamination, and has not been heard from. The third one has again a healthy vagina, and the pelvis is free from indurating masses, though the entire vaginal canal was a mass of carcinomatous growths extending up into the base of the right broad ligament and down into the fourchet.

Of the eight operable cases (Table 5) treated by surgery and radium, one patient died nine months afterward from a metastasis of the liver, another one two months later from a severe hemorrhage from the vagina. The others are at this time in a normal condition and do not show a recurrence. The average time which has elapsed since the operation is eight months.

TABLE 3.—INOPERABLE CANCERS TREATED ONLY WITH RADIUM

Case Number	Cause of Inoperability	Total Mg. Hrs. of Radium Element Applied	Duration of Treatment	Primary Results			Further Treatment	Result and Present Condition
				Refractory	Subjective Improvement	Objective Improvement		
2	Extensive involvement of vagina	9,525	5/30/14 to 9/24/14		Yes			Cauterization Nov. 3, 1913. Has vesicovaginal fistula; cachectic.
5	Involvement of entire vagina, rectum, vulva	9,900	6/ 1/14 to 8/19/14	Yes				Had colostomy. Died from exhaustion.
14	Involvement of right ureter and sigmoid	9,250	6/ 7/14 to 8/ 5/14		Yes	Yes		Aug. 5, 1914, abd. panhysterectomy; resection of sigmoid. Died Nov. 20, 1914, from carcinomatosis.
15	Involvement of parametrium and rectum	8,312	4/ 4/14 to 6/17/14		Yes			Oct. 10, 1913, colostomy. Died Jan., 1915; cancer of liver.
19	Chronic endocarditis with decompensation	3,750	7/19/14 to 8/ 9/14	Yes				Died, August, 1914, from endocarditis
21	Extensive involvement of rectum	1,125	7/29/14 to 8/ 8/14	Yes				Patient refused further treatment on account of rectal tenesmus caused by radium; had colostomy; died.
25	Cachexia and local extension of tumor	8,875	11/ 6/14 to 12/ 5/14	Yes				Died.
27	Pyosalpinx and involvement of abdominal organs	4,150	11/27/14 to 12/ 3/14	Yes				Died.
28	Extensive involvement of bladder	3,600	12/31/14 to 1/25/15		Yes	Yes	Dec. 31, 1914, cystotomy for insertion of radium	Died January, 1915, from exhaustion after hip amputation for path. fracture of femur due to metastasis.
30	Extensive involvement of bladder	2,400	1/31/14 to 2/ 2/15		Yes	Yes	Jan. 25, 1915, exploratory cystotomy	Bladder free from tumor mass; gained in weight and strength.
33	Cachexia; vagina and bladder invaded	4,800	2/ 6/15 to 2/22/15	Yes				Developed vesicovaginal fistula; refused to continue treatment. Died.
36	Pyometra.....	2,925	3/12-23/15 to 3/22/15		Yes	Yes		Cervix now normal.
37	Involvement of bladder	1,700	3/15/14 to 3/20/15	Yes			March 8, 1915, exploratory laparotomy	Had a thrombophlebitis. Exacerbation. Died from septicemia.
31	Extensive involvement of rectum	4,800	2/12 to 4/ 2		Yes	Yes		Rectum normal and freely movable. Returned to work.

TABLE 4.—RECURRENT CANCERS

Case Number	Date of Primary Operation	Character of Operation	Date of Recurrence	Condition of Pelvic Organs	Total Mg. H. of Radium Element Applied	Duration of Treatment	Primary Results			Remarks and Results
							Refractory	Subjective Improvement	Objective Improvement	
3	July, 1910	Vaginal panhysterectomy	June, 1914	Nodule and ulcer size of bean in vaginal vault	10,350	7/27/14 to 11/30/14		Yes	Yes	Patient succumbed to an intercurrent disease, March, 1915; cauterization 7/31/14.
8	Jan. 9, 1913	Abd. hysterectomy	Sept. 1913	Involvement of entire vagina	5,700	4/ 6/14 to 5/28/14		Yes		Vesicovaginal fistula. Died Sept. 21, 1914, from exhaustion.
10	Sept. 16, 1913	Vag. cauterization	Oct. 1913	Involvement of vagina, vulva and perineum	3,375	4/25/14 to 5/13/14	Yes			Septicemia after third radium treatment. Died May, 1914.
13	May	Vag. hysterectomy	Apr. 1914	Involvement of entire vagina	2,275	6/13/14 to 6/15/14		Yes	Yes	Vagina healed immediately; did not return for treatment.
20	Aug. 12, 1912	Vag. hysterectomy, salpingo-oophorectomy sinistra	Mar. 1914	Mass involving right adnexa	3,500	7/10/14 to 7/13/14	Yes			Developed vesicovaginal intestinal fistula; succumbed to exhaustion August, 1914.
26	Sept. 2, 1914	Abd. panhysterectomy	Nov. 1914	Ulcer in vaginal vault	2,300	11/23/14 to 11/25/14	Yes			Nov. 23, 1914, cauterization of vag. vault; developed intestinal fistula; died Dec. 27, 1914; exhaustion.
32	Oct. 1913	Vaginal hysterectomy	Apr. 1914	Ulcer in vaginal vault involving right parametrium and bladder	5,175	2/15/15 to 3/23/15	Yes			April 20, 1915, tumor increasing in size; patient loses weight and strength; has much pain.
34	Fall, 1914	Abd. panhysterectomy		Mass involving vag. vault extending to right up to brim	2,800	3/ 9/15 to 3/20/15	Yes			Losing weight and strength.
35	March, 1914	Vag. and abd. panhysterectomy	Aug. 1914	Ulcer involving entire vagina and right parametrium	3,900	3/10/15 to 4/ 6/15		Yes	Yes	April 30, 1915, vagina and vulva normal and free of any nodular masses.
45	4/25/15	Percy cautery	Never; compl. recovery	Crater involving parametria	3,950	6/ 1/15 to 6/12/15		Yes		

HISTOLOGIC FINDINGS

The action of the gamma rays on carcinoma tissue has been studied in eight cases, namely, six uterine (Cases 12, 14, 16, 24, 29 and 39); one rectal (Case 31), and one skin cancer (Case 85). The latter has been added, as it affords a particularly favorable instance for the study of the changes occurring in carcinoma cells by the action of radium. The reproductions of the first microscopic sections (Figs. 1 and 6) were made from tissues removed from the tumor before the beginning of the radium treatment. The time of removal of the other sections is stated beneath each illustration; also the amount of radium element applied preceding the removal of the sections, and the time duration of the application of each course.

The histologic changes may be divided into four stages:

The first stage is characterized by an enlargement of the carcinoma cells, a hyperchromatosis and a pyknosis of the nuclei. They are evident in all the cases examined. These changes usually occur within about

Case 12 there was evidence of a completely destroyed cancer tumor, yet the patient succumbed to a bowel invasion, proving that some cancer cells either remained uninfluenced by the radium or regenerated after the subsidence of the action of the rays. Therefore, certain questions arise which call for definite answers before we can positively state that radium rays cause a degeneration and ultimate death of cancer tissue and a simultaneous regeneration of connective tissue.

1. Are we able by histologic examination to differentiate the necrobiotic changes in the carcinoma cells brought about by natural and artificial conditions from those caused by the influence of radium rays? It is evident that we cannot do so. Cells undergo necrobiotic changes in the course of their existence. Heat, caustics and alcohol, brought in contact with the tissues, may produce the same changes, as is well known. However, such general and extensive changes as seen in these specimens, the absence of cell degeneration as evidenced in the first sections, and, finally, the regu-

TABLE 5.—CANCERS TREATED BY SURGERY AND RADIUM

Case Number	Date of Operation	Character of Operation	Complications of Convalescence	Mg. Hrs. of Radium Element Applied	Duration of Radium Treatment	Result	Remarks and Present Condition
1	9/25/14	Abd. panhysterectomy; vag. cauterization	Vesico-abd. and vesicovag. fistula	4,400	10/10/14 to 10/26/14	Perfect recovery	Died two months afterward from a vaginal hemorrhage.
4	8/26/14	Vag. cauterization; abd. panhysterectomy	Vesicovaginal fistula	6,775	9/ 6/14 to 10/13/14	Recovery, but fistula recovered.	Well, April, 1915; fistula closed.
6	7/17/14	Perineal cystotomy and cauterization	None	3,150	8/ 3/14 to 9/ 1/14	Recovered....	
7	7/ 2/14	Resection of 8" of rectum; perineal operation	None	2,175	7/16/14 to 8/ 1/14 and 10/30-31/14	Recovered....	Dying from metastatic cancer of liver.
17	4/20-24/14	Vag. cauterization; abd. panhysterectomy	None	3,525	5/15/14 to 5/30/14	Recovered.	
24	10/29/14	Abd. panhysterectomy...	None	4,150	10/21-23 and 11/11-13/14	Recovered....	Oct. 21, 1914, diagnostic curettage; well.
38	3/16/15	Abrasion of mucosa; amputation of cervix....	None	2,550	3/21 to 3/28/15	Recovered.	
41	4/16/15	Abdominal hysterectomy; vag. cauterization; abd. panhysterectomy	None	3,950	4/19 to 5/4		Extensive involvement of anterior vaginal wall. Really an inoperable case; impossible to remove entire growth.
44	5/20/15	Abd. panhysterectomy; cauterization	None	4,000	5/23-31/15		Extensive involvement of right parametrium; impossible to remove entire tumor mass.

ten days after the first application of radium (Figs. 3 and 7).

In the second stage we observe karyolysis, karyorrhexis, cytolysis and cell detritus. Figure 3 shows many evidences of such changes. They are observed as early as from the first to the third week of the treatment.

The third stage shows an absorption of the cellular and nuclear debris by phagocytes. Macrophages and microphages are concerned in this step. Microphagic activity is highly evident in Figure 3, while macrophages are seen to be active in Figure 8.

The fourth stage is the stage of connective tissue proliferation and scar formation. It completes the histologic cure of cancer. The places left vacant by the dead carcinoma cells are immediately filled by young fibroblasts derived from the connective tissue stroma of the tumor. The fibroblasts become differentiated. Figure 4 shows the connective tissue regeneration. The fourth stage appears usually after from the first to the third month, but may occur much sooner.

A difference frequently exists between the clinical results and the histologic findings. For instance, in

larity of their occurrence in all the tissues investigated, even in those not previously cauterized, permit us to state that they must be caused by the action of the gamma rays.

2. Can we, by examination of small pieces of tissue removed from the growth, determine the extent and intensity of the action of radium rays? We cannot from such an examination, but could do so from serial sections of all the organs removed either intra vitam during operations, or, preferably, postmortem.

I have, fortunately, four cases in which an abdominal panhysterectomy was performed after a clinical cure of the cancer by the use of radium rays was obtained (Cases 12, 14, 16 and 24). Serial sections were made from the tissues removed. A microscopic examination revealed that the cytolytic changes were generally present throughout the organs removed. This does not prove that distantly located foci were not left behind. As a matter of fact, Patients 12 and 14 died subsequently from cancer. This shows that viable cancer cells were left behind somewhere in the pelvis. Bumm examined tissues acted on by gamma rays and removed afterward during postmortem examinations. He estimated that the intensity of the gamma rays

sufficient to destroy carcinoma tissue extended into a radius of 4 cm. Within this area of intensity, carcinoma cells were not found present; beyond it, however, typical unchanged cancer cell nests were still found to exist. In other words, extensive carcinoma growths are only partially destroyed by gamma rays. This area of destruction, however, has a diameter of 8 cm., and enables us to reach tissues which a knife could never remove.

3. Is it possible by such microscopic examinations to state whether a carcinoma cell has perished or whether it might not regenerate after the action of the radium rays ceases? The following citation will illustrate the answer to this question: Chéron and Rubens-Duval treated a patient suffering from an inoperable carcinoma of the cervix with radium during November, 1910, and January, 1911. The patient was apparently clinically cured. She died from an intercurrent disease (a cerebral softening) during April, 1912, fifteen months after the beginning of the radium treatment. All the internal organs and tissues were removed postmortem, and a careful serial histologic examination of all the tissues did not reveal a single carcinoma cell at any place of the organism. A complete anatomic cure by radium rays has thus been demonstrated.

My investigations demonstrate the uniformity and general extent of the necrobiotic changes brought about in the carcinoma cells by the action of the gamma rays. Bumm's researches fix the extent of the area of intensity of the rays within which a carcinoma will become destroyed, and Chéron and Rubens-Duval's case proves the capability or efficiency of the radium rays to bring about an anatomic cure of cancer.

CONCLUSIONS

1. The best method of applying radium is the interval method by which from 3,000 to 4,000 milligram hours of radium element are applied within from about fourteen to twenty-one days.

2. The alpha and beta rays must be arrested by a brass filter of from 1 to 1.5 mm. thickness.

3. The secondary rays, forming in the metal filter, are rendered inert by a rubber cot of from 1 to 3 mm. thickness.

4. Inoperable cancers that are not far advanced so that cauterization is not contraindicated yield satisfactorily to radium therapy.

5. Advanced inoperable and recurrent cancers are ordinarily refractory toward the radium rays. Any improvement is at least very temporary.

6. The patients treated with the rays after surgical removal of the organs have done well, although the time elapsed since the treatment averages eight months.

7. Patients suffering from cancer should be treated surgically and then radiologically, and if surgery is contraindicated they should receive radium treatment, which at least relieves the subjective symptoms and often the objective ones.

8. The time elapsed since the commencement of the radium treatment in all the cases enumerated is too short to permit definite opinion as to the remote results of radium treatment.

9. Clinical and histologic studies enable us to pronounce the radium rays a valuable addition to the therapy of cancer.

10. It will require years of constant observation to demonstrate such results as anatomic cures.

11. The same measure that is applied to establish the efficacy of surgical procedures in cancer treatment must certainly be employed in radiotherapy.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. BURNAM AND KELLY, AND SCHMITZ

DR. J. F. PERCY, Galesburg, Ill.: Ewing of New York said a few years ago that the balance in cancer is easily upset; and this must be true, because there are a number of methods of destroying or inhibiting cancer that have a certain number of clinical cures to their credit. It would be interesting if we could go back in a historical way to these various methods and determine just how much they have accomplished. One thing has been brought out by both of these papers, and that is the totally inexplicable way some cases are clinically cured and other cases apparently of the same type are either made worse or not affected by the same treatment. The problem of the treatment of inoperable cancer of the uterus has always been of the gross mass, and it is a question whether or not radium, in the great mass of cancer usually seen in the cervix, is as valuable as some other method that will at once, or in a comparatively few minutes, get rid of this gross mass. Another problem is the metastasis, and I am glad that both the essayists have mentioned an immunity, or, at least, suggested it. This immunity is undoubtedly developed in greater or less degree, and without doubt takes care, in many cases, of the metastases after the destruction of the gross mass. At least I am convinced of this from my own experience. I am especially interested in the destruction of the gross mass by heat. I am convinced that this method is the most certain of any of the methods that have been brought to our attention. In addition, it does not require specialized judgment and the apparatus required is comparatively inexpensive. One of the difficulties of radium and the Roentgen ray in attacking the gross mass of cancer is that they break down a lot of cancer cells, and if drainage is not provided, an overdose of the broken-down cancer cells may be absorbed and kill the patient. In other words, even with radium or the Roentgen ray, if one attacks the gross mass he must provide for some form of drainage. This is easily done with the heat technic. It is not easily done with either radium or the Roentgen ray.

DR. S. M. D. CLARK, New Orleans: The two papers show definitely that we are not marking time in the warfare on cancer. We are beginning to see rays of light, and I feel confident that if the present pressure is kept up, our results will progressively improve. I am sorry that I cannot discuss the subject from the radium point of view, but since I note that the best results obtained by one of the essayists was when using the radical operation after the growth had been transformed by using radium, it seems appropriate to consider cancer of the uterus from another angle.

Though the Percy heat method has great merit, still when viewed in the light of a cure, it falls short and is to be looked on more as an adjunct or link in the chain of treatment. Time is too short to go into the detail of my combination method, but its chief point rests in being able to transform inoperable into operable cases by performing the work as a two-stage operation. At the first sitting the abdomen is opened and both internal iliacs and one ovarian artery are tied, primarily for the purpose of starving the growth, as well as to control secondary hemorrhage. Heat is applied at the same time. After three to five weeks' interval the patient is transformed constitutionally and locally, when the radical removal is done. This method increases operability and decreases the primary mortality. If we keep accurate records of our work, in ten years stock can be taken of our results, and the best method adopted.

DR. HENRY SCHMITZ, Chicago: It is a question of developing first the therapy, and second the technic of the application of radium. If we do know the amount and the manner in which we should use it, our results will improve. My first cases treated were not so successful as at present. I feel

that radium will do more in the eradication of cancer than any other means. I have applied surgery, heat and everything I possibly could use, but since I have been using radium I feel more confident of benefiting my patients.

DR. CURTIS F. BURNAM, Baltimore: I omitted one thing that I intended to say, that in the beginning we catheterized and curetted our big masses. More recently we are not doing that. So far as I know, there is no general upset in the treatment. We give a single treatment, and repeat it in six weeks if the growth is still there. If it has gone, we wait three months; but if it has not gone we repeat; and the patient rarely stays in the hospital longer than the day of treatment.

THE ROENTGEN-RAY TREATMENT OF SKIN DISEASES *

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THE DERMATOLOGIST AND THE RADIOLOGIST

Now that Roentgen-ray work is becoming highly specialized, there seems to be a tendency to separate

Fig. 3.—A group of hypertrophic lichen planus papules on the wrist. Also two common warts, one on the little finger and one at the base of the index finger.

dermatology from roentgenotherapy. This is both desirable and undesirable. So far as concerns the Roentgen-ray treatment of skin diseases, two general attributes are essential—a knowledge of dermatology and skill in modern Roentgen-ray technic. The dermatologist possesses the former and he can easily acquire the latter, for the difficulties are more imaginary than real. The pure roentgenologist, while being expert in Roentgen-ray technic, lacks a dermatologic training, as also do many of the physicians who refer patients to him for treatment. To avoid errors in diagnosis and the obvious consequences, it would seem advisable to adhere to one of three schemes: for the dermatologist to employ the Roentgen ray; for the roentgenologist to have at least a clinical knowledge of dermatology; or for both to combine their skill in behalf of the patient.

TECHNIC

In a short, practical paper of this kind it is not possible actually to describe a technic. A general out-

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* On account of lack of space this paper has been abbreviated for THE JOURNAL. It will appear in full in the Transactions of the Section and in the author's reprints.

line of modern methods may, however, be of interest. Two methods are in vogue at the present moment, namely, intensive and divided doses.

Intensive Method.—Here the quality of the ray used is ascertained by direct measurement (Benoist, Walter or Wehnelt instruments), while it is maintained by means of indirect measurement (milliamperemeter, spark-gap, etc.). The quantity is measured directly, through the employment of reliable radiometers such as those originated by Holz-

Fig. 4.—Same as Figure 3 after one dose of H 4, B 9 was applied to the lichen lesions. Note the area of temporary pigmentation at the wrist. Note also that the warts have disappeared without having been exposed to the ray.

knecht and Corbett. In this way every dose is estimated as accurately as modern science will allow. An intensive treatment may consist of enough rays to produce a second degree Roentgen dermatitis, a simple erythema, a loss of hair without erythema, or a dose that is too small to produce a visible effect on the normal skin, but yet too large to allow of its repetition within three or four weeks. The method is thoroughly established and is sufficiently accurate for all practical purposes. No better example of its accuracy can be demanded than the excellent results associated with the intensive Roentgen-ray treatment of ringworm and favus of the scalp.

There is a difference of opinion regarding the quality of ray to be employed in different cutaneous diseases. Contrary to

Fig. 5.—Chronic eczema with acute exacerbations.

the general consensus, I have found a "hard" ray (B 8 to 10) preferable for routine work and seldom use a ray of lower penetration.

In considering the quantity, the question of idiosyncrasy and susceptibility should be discussed. True idiosyncrasy must be a very rare phenomenon. Again I direct attention to thousands of cases of tinea tonsurans that have been treated