

COBALT-60* TELETHERAPY FOR COMPLICATED PEPTIC ULCER

A Preliminary Report

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ROENTGEN THERAPY to the fundus of the stomach was first used 40 years ago by Bruegel¹ in the treatment of peptic ulcer. Palmer and associates²⁻⁴ have used irradiation extensively during the past 20 years as one aspect of ulcer therapy that included a strict medical regimen consisting of a bland diet, frequent feedings, antacids, sedation, psychotherapy, and other measures. In 1948 they³ reported follow-up studies on 800 patients, and to date approximately 1200 of their patients with peptic ulcer have received such therapy.² Their follow-up studies have revealed excellent results, with a low incidence of recurrent peptic ulcer, which have stimulated our interest in the adjunctive use of irradiation in the treatment of complicated peptic ulcer.

Gastric secretory studies are most important in evaluating any treatment for peptic ulcer. It has been repeatedly stressed, "No acid, no ulcer." Any type of therapy that results in an acidity will be effective ulcer treatment. In 1939, Palmer and Templeton⁴ reported a transitory reduction in acid secretion in all cases receiving roentgen therapy. In 35 of 88 patients studied, achlorhydria occurred. Ricketts, Kirsner, Humphreys, and Palmer⁵ found a reduction in volume of gastric secretion averaging 47.5 per cent, with complete anacidity in 13 of 15 patients with gastric ulcers who had received a depth dose of 1600 r. With their latest technic (Technic A) and with a depth dose of 1600 to 2500 roentgens, 44 (76 per cent) of 58 patients developed achlorhydria, and an additional 6 (11 per cent) had a 50 per cent or more reduction in acid secretion. They²⁻⁴ found that larger doses of irradiation were more effective in producing anacidity. This effect of different doses was further indicated in the report by Brown and associates⁶ that in only 3 of 12 patients anacidity followed irradiation with 1500 r, but in 6 of 10 patients anacidity followed irradiation with 2000 r. All of these secretory studies have shown that: (1) Irradiation results in depression of gastric secretion and frequently in anacidity. (2) There is correlation between

*The radioactive material used in this study was supplied on authorization of the Isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tennessee.

the degree of reduction of acidity and the amount of irradiation administered. (3) The decrease in acid secretion may persist for varying periods. (4) While the acid secretion remains depressed, the ulcer heals and does not recur.

Technics of irradiation. Various technics of irradiation have been used. McGeorge⁷ used radium needles in the stomach, giving 2000 to 3000 milligram-hours. Sixteen of his 32 patients developed achlorhydria, while 28 of 30 patients showed reduction in the amount of free acidity, and 29 of 30 had reduction in volume of secretion. Brown and associates⁶ initially used only roentgen irradiation in 22 patients. Of 10 patients who received 2000 r, 4 had severe relapses (3 required surgical treatment). Subsequently, these investigators combined roentgen with surgical (antroduodenectomy) therapy in 10 patients. The preliminary results of combined irradiation and surgical treatment were excellent in the limited follow-up period of three months. A much longer period of follow-up, as the writers point out, is necessary for proper evaluation. Four technics of roentgen therapy have been used by Palmer and associates.^{2,3} With their latest technic² a barium swallow outlines the stomach fluoroscopically so that irradiation may be directed at the upper two thirds of the stomach in which there is the greatest concentration of acid-secreting cells. The depth doses are 1600 to 2500 r through two portals, anterior and posterior.

Ricketts, Palmer, Kirsner, and Hamann³ in an analysis of 800 cases of peptic ulcer treated in the years 1936 to 1947, reported that the recurrence rates of gastric and duodenal ulcer were lower in the group of patients that had received roentgen therapy than in the group that had not received irradiation. They concluded that, in the treatment of peptic ulcer, irradiation of the acid-secreting portions of the stomach was a valuable procedure, the effect being proportional to the reduction in gastric secretion. As they further indicated, the use of radiation therapy for peptic ulcer is based on the concepts of the relationship of acid gastric secretion and chronic peptic ulcer, and the depressant effect of roentgen irradiation on gastric secretory capacity.

Since September 1954, irradiation with the cobalt-60 teletherapy unit has been used at the Cleveland Clinic. The present report is based on the results of administering cobalt-60 teletherapy to 15 patients having complicated peptic ulcer. We believe that this is the first report on the use of cobalt-60 teletherapy for this purpose.

Technic

In general we have followed the procedure that was originated by Palmer and his group²⁻⁴ for the administration of roentgen irradiation to the stomach for peptic ulcer. However, instead of the usual 200- or 250-kv. roentgen ray machines, we use a cobalt-60 teletherapy unit (equivalent to 3000 kv. or 3 million volts).

The patient is given a small amount of barium orally, and is fluoroscoped in both the prone and supine positions. The upper two thirds of stomach is outlined on the skin while the patient is in the prone and supine positions since these are the positions he will assume on the therapy table.

Two fields, one anterior and one posterior, centered over the upper two thirds of the stomach, are employed. This effectively cross-fires the acid-bearing portion of the stomach. From 1600 to 2000 r to the stomach were given through these two portals to each of our 15 patients (Table 1). We space the treatments fairly closely, giving 300 r to the skin of each of the two fields daily for six to eight days.

Table 1.—*Effect of cobalt-60 teletherapy on gastric acidity*

Diagnosis	Case no.	Dose of Co ⁶⁰ , r	Gastric acidity		Decrease in free HCl, %	Length of time since therapy
			Before therapy, units	After therapy, units		
Duodenal ulcer	1	1600	102/114	10/36	90	8 wk.
	2	1664	74/90	12/22	89	6 wk.
	3	1600	110/122	00/26	100	8 wk.
	4	1800	109/121	24/56	88	6 wk.
	5	1840	22/32	00/12	100	8 wk.
	6	1600	90/112	50/68	44	8 wk.
	7	1700	60/72	40/62	37	3 wk.
	8	1800	98/110	58/74	43	8 wk.
	9	1800	120/136	14/24	88	9 wk.
	10	1800	92/108	20/30	78	8 wk.
	11	2000	114/126	76/90	32	8 wk.
Marginal ulcer	12	1600	68/82	62/72	10	6 mo.
	13	1600	Not determined			
	14	2000	46/62	00/18	100	8 wk.
Gastric ulcer	15	2000	118/128	14/28	89	8 wk.

The cobalt-60 teletherapy unit has certain physical advantages over the conventional roentgen ray therapy machines. In particular, it has a skin-sparing effect and, being more penetrating, a greater depth dose is obtained. We believe that there is no difference between the biologic reaction to the gamma rays of cobalt-60 and that to the roentgen rays of a 250-kv. roentgen ray machine. In the average patient, measuring approximately 22 to 24 cm. in anteroposterior diameter, a 50 per cent depth dose at 11-cm. depth is obtained with the cobalt-60 equipment. To deliver 2000 r to the desired portion of the stomach, 2000 r must be administered to the skin of each of the two fields. This dose together with an exit dose of approximately 600 r means that the skin fields receive approximately 2600 r, but no noticeable skin reactions have resulted. A similar amount of conventional roentgen irradiation would cause a mild

erythema. We consider that with benign conditions we are not justified in giving treatment that can cause a skin reaction, particularly in patients of the younger age group.

In addition to cobalt-60 teletherapy, the patients were treated medically as outlined by Brown and Hoerr.⁸ They were given a generous, bland diet that includes meat and cooked vegetables and between-meal food or milk every two hours from arising to retiring, antacids on the odd hours when they were awake, mild sedation in the form of phenobarbital, and one of the anticholinergic drugs.

The patients were not hospitalized, but were given the teletherapy as outpatients. Although hospitalization offers rest and a beneficial change in environment to a patient with peptic ulcer we believe that, given adequate instruction, he can adhere to his medical program of hourly feedings or antacids carefully at home.

Selection of Patients

The 15 patients selected for cobalt-60 teletherapy had not responded to previous medical treatment, had evidence of complications of peptic ulcer or of intractability, and were considered to be possible candidates for operation. Surgical treatment was not advised or performed because of various contraindications such as cardiac disease, or because of the reluctance of the patient to undergo operation. Operation was cancelled for one patient when he became cyanotic on the operating table before any surgery. Cobalt-60 teletherapy was given in addition to the medical treatment in the hope that operation might be avoided.

The duration of ulcer distress ranged from 2 to 30 years, with an average of 12 years of intermittent ulcer pain (Table 2). Six of the 15 patients had had one episode of massive bleeding, and one had had three episodes of minor bleeding. Three patients had obstruction and vomiting, and a fourth patient had obstruction with a dilated stomach and no vomiting. Eleven of the patients had duodenal ulcer. Of three patients with marginal ulcer, two had had two operations for peptic ulcer previously (Table 2, Cases 12 and 14).

Results

Pretreatment and posttreatment white-cell counts and hemoglobin determinations showed no significant change.

Clinical response. The clinical response of peptic ulcer to any type of therapy is difficult to evaluate because of our limited knowledge of the natural history of untreated peptic ulcer, and the latitude in patient self-treatment and professionally administered therapy. In cases of duodenal ulcer many patients undoubtedly treat themselves, with or without the help of the local druggist, using measures such as control of diet and doses of soda and proprietary antacids. Probably only those patients with stubborn or complicated ulcers who

Table 2.—Response to cobalt-60 teletherapy in 15 patients having peptic ulcer

Diagnosis	Case no.	Duration of symptoms, yr.	Symptoms	Previous surgical treatment	Response to cobalt-60 teletherapy	Length of follow-up, mo.
Duodenal ulcer	1	27	Pain, vomiting	None	Asymptomatic	4
	2	7	Pain, hemorrhage, melena	None	Asymptomatic	3
	3	2	Ulcer distress, melena	None	Asymptomatic	4
	4	10	Obstruction, pain, melena	None	Asymptomatic	4
	5	14	Pain, vomiting, melena	None	Asymptomatic	4
	6	10	Pain, hematemesis	None	Asymptomatic	2½
	7	5	Pain, vomiting	None	Asymptomatic	2
	8	2½	Recurrent ulcer	None	Asymptomatic	2
	9	30	Recurrent ulcer	None	Asymptomatic	2
	10	3	Pain, not working for 9 mo.	None	Asymptomatic	2
	11	8	Pain, melena	None	Asymptomatic	2
Marginal ulcer	12	10	Severe pain	Gastric resection, Jan. 1953; vagomy, Aug. 1953	Asymptomatic	8
	13	15	Pain, 3 episodes of melena	Vagotomy and gastroenterostomy, 1952	Asymptomatic	16
	14	15	Pain, requiring narcotics	Gastrojejunostomy, 1947; vagotomy, July 1956.	Asymptomatic	2
Gastric ulcer	15	15	Recurrent pain	None	Asymptomatic	2

have not responded to home remedies or to treatment by their local doctors are referred to medical centers. Consequently, the group that is seen in large clinics is a selected one. In addition, irradiation is not used alone, but is combined with other types of therapy, such as diet, frequent feedings, antacids, sedation, antispasmodic and anticholinergic drugs, and psychotherapy, and it is therefore difficult to evaluate the effect of irradiation alone.

The long histories of ulcer in the group, the number of complications, and the lack of response to previous medical (in three cases also surgical) treatment are some measure of control. Follow-up periods have been short, ranging from 2 to 16 months. During this time the symptomatic response has been satisfactory in every case (Table 2). In each patient there has been relief of ulcer distress, and no further hemorrhage or other complications.

Gastric acidity. Gastric analyses, using Histalog (3-beta-aminoethylpyrazole dihydrochloride) as a stimulant, were obtained before and after irradiation in 14 of 15 patients. According to Kirsner, Levin, Palmer, and Ford,⁹ Histalog is

Chart.—*Per cent decrease in free HCl after cobalt-60 teletherapy*

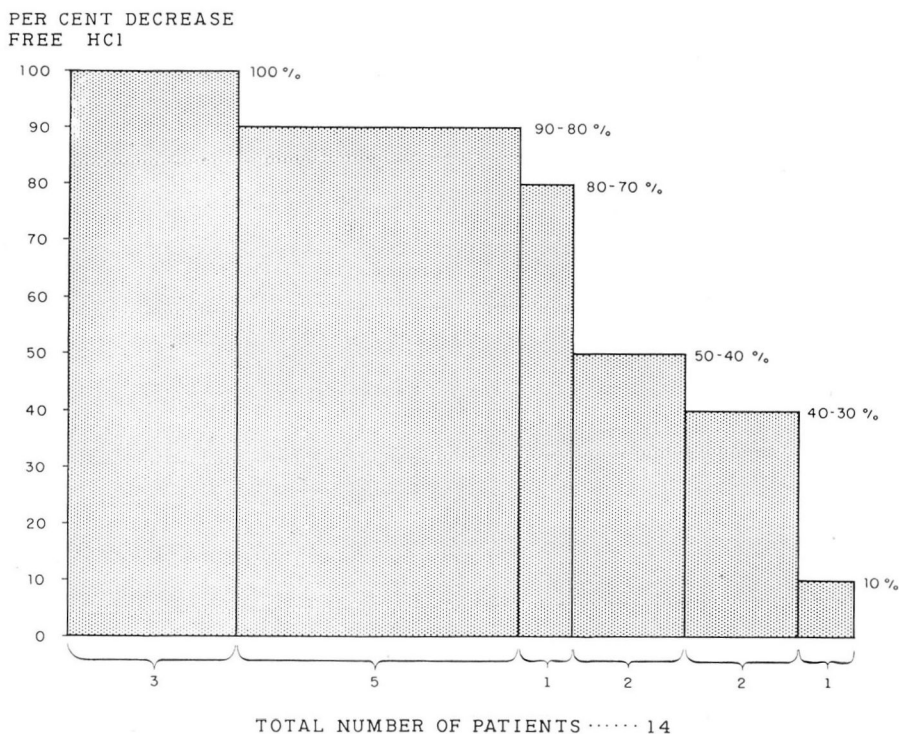


Chart depicting the percentage decrease in free hydrochloric acid after cobalt-60. All gastric analyses were done with Histalog as a stimulant. From the chart it can be seen that 8 of 14 patients had an 80 per cent or greater reduction in free hydrochloric acid.

entirely comparable to histamine in stimulating gastric-acid secretion. Fifty milligrams (one ampule) of Histalog was given to each patient in a fasting state. The results of the analyses are summarized in Table 1.

Thirteen of the 14 patients had an appreciable reduction in gastric acidity, greater than 32 per cent. Nine of the 14 patients had a reduction in gastric acidity of more than 75 per cent (Chart). Anacidity was produced in three patients. More frequent gastric analyses after irradiation might have shown a higher incidence of anacidity, since this anacidity frequently is temporary. Gastric analysis could not be obtained in Patient 13 (Table 1) until six months after irradiation, when it showed little change. However, the marked symptomatic improvement in this patient suggests that he had at least a temporary decrease in acidity. Despite the small number of patients and of determinations of secretory response, we believe that these studies show that irradiation with cobalt-60 may appreciably decrease gastric-acid secretion.

Roentgen findings. Progress roentgen examinations were made of 13 patients (all except Cases 6 and 13, Table 3). In each the ulcer crater disappeared.

Table 3.—*Roentgen findings before and after cobalt-60 teletherapy*

Diagnosis	Case no.	Roentgen findings		Length of time after therapy
		Before therapy	After therapy	
Duodenal ulcer	1	Crater	Deformity only	2 mo.
	2	Crater	Deformity only	6 wk.
	3	Crater	Deformity only	2 mo.
	4	Crater, obstruction	Deformity only	10 wk.
	5	Crater, obstruction	Deformity only	2 mo.
	6	Crater	Not available	—
	7	Crater	Deformity only	2 mo.
	8	Large ulcer crater	Crater healed	9 wk.
	9	Crater	Less deformity, no crater	9 wk.
	10	Large crater	No crater	8 wk.
	11	Crater	Crater healed	8 wk.
Marginal ulcer	12	Large marginal ulcer	Normal stoma	2 mo.
	13	Crater	Not available	—
	14	Large marginal ulcer	Normal stoma	8 wk.
Gastric ulcer	15	Crater, lesser curvature of antrum	Crater healed	8 wk.

Side effects of therapy. Twelve of the 15 patients tolerated the therapy without side effects. Three patients had minimal nausea but no vomiting while undergoing therapy. The degree of nausea was much less in these patients than in those who, prior to the use of cobalt-60, were given comparable doses or

roentgen irradiation to the stomach for peptic ulcer. No skin changes were noted in any of the patients.

Discussion

Gastric secretory studies in 14 of the 15 patients having peptic ulcer showed a reduction in acidity in 13 after cobalt-60 teletherapy (1600 to 2000 roentgens). This reduction was greater than 75 per cent in 9 of the 14 patients. Our experience supports that of other investigators who showed that with larger doses of irradiation a greater depression of acid secretion results. For further studies we plan to give approximately 2000 roentgens.

The effect of roentgen therapy can be measured directly by determining gastric-acid secretion. Frequent gastric-acid determinations will aid in estimating both the expected response to the treatment and the possible value of cobalt-60 teletherapy for all patients having ulcer. We are planning follow-up studies that will include gastric-acid determinations every two months for the first six months after irradiation, and twice yearly thereafter.

Histologic findings. The histologic findings after irradiation have been reported by several investigators.^{5-7,10} Ricketts and associates⁵ reported gastroscopic and gastric biopsy findings after irradiation in patients having peptic ulcer. Goldgraber and associates¹⁰ made extensive studies of three patients undergoing roentgen therapy for duodenal ulcer. With a modified Wood biopsy tube, they performed 40 biopsies within a four-month period. The histologic changes were of a patchy nature. Initially, coagulation necrosis of the fundal glands occurred, involving both the chief and the parietal cells. At the peak of reaction, there was partial to complete loss of glandular substance, with mucosal thinning, edema, and chronic inflammatory infiltration of the mucosa. The reversion to normal was complete and prompt. Brown and associates⁶ evaluated the response to irradiation on the basis of 138 gastric biopsies with the Wood instrument. McGeorge's⁷ findings were similar: an initial necrosis followed by an inflammatory reaction in five patients who had undergone gastrectomy after irradiation.

Gastric ulcer and cobalt-60 teletherapy. In this study, we have included only one patient having gastric ulcer. Patients with gastric ulcer have less acid secretion than do those with duodenal ulcer. Levin and associates^{2,11} found that postirradiation anacidity develops more frequently and that irradiation produces better results in patients with gastric ulcer than in those with duodenal ulcer. We are planning to study the effects of this type of therapy on more patients with gastric ulcer.

Summary

The results of administering cobalt-60 teletherapy to the stomach in 15 patients having peptic ulcer are encouraging. The doses ranged from 1600 to

2000 r and were well tolerated causing no skin changes or other side effects, except minimal nausea. Since irradiation with cobalt-60 is better tolerated than is the conventional roentgen treatment, it is suggested that irradiation with cobalt-60 is preferable. Gastric-acid secretion was significantly reduced in 13 of 14 patients, and 3 of the 14 developed anacidity.

There was a good symptomatic response in all patients. Before cobalt-60 teletherapy, all 15 patients had symptoms of complicated peptic ulcer and had not responded to medical treatment. The good symptomatic responses strongly suggest that irradiation was beneficial.

Progress roentgen examinations in 13 patients showed the ulcer craters to have disappeared within 6 to 10 weeks after irradiation.

The results of this short-term experience indicate the desirability of further use of cobalt-60 teletherapy as an adjunct to the treatment of patients with peptic ulcer resistant to other medical regimens.

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