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COMPLICATED PEPTIC ULCER TREATED BY COBALT-60* TELETHERAPY

A Preliminary Report of Results in 34 Patients

CHARLES H. BROWN, M.D.**

During the last three years, cobalt-60 teletherapy has been used at the Cleveland Clinic in conjunction with intensive medical treatment in 34 patients having complicated peptic ulcer. Since a long-term follow-up always is necessary to evaluate properly any new type of therapy for peptic ulcer, this paper is only a preliminary report.

The use of irradiation in the treatment of peptic ulcer is not new, and various technics have been employed to deliver the irradiation to the stomach itself. Previously, we have treated a few patients with a 250-kv. roentgen ray machine. Irradiation by means of cobalt-60 teletherapy unit¹, as we have used it, has been an adjunct to conventional therapy² and has not replaced diet, sedation, antacids, and anticholinergic drugs.

The goal of irradiation of the stomach is to decrease acid secretion. Numerous studies have shown that roentgen irradiation at least temporarily decreases gastric acid secretion and frequently results in anacidity³. Roentgen therapy for peptic ulcer was first used by Bruegel⁴ in 1917 and since has been used by a number of workers. Palmer, Kirsner, and their group at The University of Chicago have employed this form of therapy more extensively than any other group⁵⁻⁷. Levin, Clayman, and Palmer⁸ reported the results in 723 patients treated from 1937 to 1950 and followed to January of 1956. The recurrence rate of symptoms per 100 patients' years was 102 before treatment and was 17 after treatment. The recurrence rate of hemorrhage was reduced from 4.3 before to 1.1 patient years after treatment and perforation from 0.2 before to 0.1 after treatment. They noted no serious side effects of irradiation. Some patients had erythema of the skin and subsequent tanning, but none developed leukemia. Their study with its long follow-up indicates that the results from the combined use of irradiation and rather strict medical treatment are excellent.

Various technics of irradiation have been used. McGeorge⁹ has placed radium needles in the stomach. Brown and associates¹⁰, in England, combined irradiation with antroduodenectomy. Palmer's technic⁸ has been to administer 1800 to 2500 roentgen units to the fundus of the stomach through two portals with a 250-kv. machine. The stomach is outlined fluoroscopically before therapy is started. Conventional medical therapy also is given to these patients.

It has been repeatedly stressed "No acid, no ulcer." Any therapy that results in anacidity will be effective ulcer treatment, and even treatment that causes a

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reduction in acidity may be effective. Previous studies have shown:

1. Irradiation depresses gastric secretion.
2. There is a correlation between the degree of reduction of anacidity and the amount of irradiation given.
3. The decrease in acid secretion may persist for varying periods of time. In a few patients the depression of gastric acid secretion may be permanent but in most patients it is only temporary.
4. While the acid secretion is depressed, particularly if anacidity occurs, the ulcer heals; and the ulcer does not recur until and unless the acid secretion returns.

The technic of irradiation employed in our patients was adapted from that of Palmer,^{5,8} except that the cobalt unit was used instead of the roentgen ray machine. While most of Palmer's patients were hospitalized, ours were treated as out-patients. The stomach was outlined by barium fluoroscopically and marked on the skin anteriorly and posteriorly in two fields. These two fields were centered over the upper two thirds of the stomach and were employed for the irradiation. It should be noted that the irradiation is given to the upper two thirds of the stomach, which is the acid-secreting portion, and not to the ulcer itself. Each patients received a total of approximately 2000 roentgen units (depth dose).

The cobalt-60 teletherapy unit has certain physical advantages over the conventional roentgen ray machine. 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 the reaction to the roentgen rays of the 250-kv. roentgen ray machine.

In addition to irradiation the patients were treated medically² on an intensive ulcer program. This consisted of a liberal diet, but with food or milk every two hours on the even hours, antacids on the odd hours, mild sedation and anticholinergic drugs.

SELECTION OF PATIENTS

The 34 patents selected for cobalt-60 teletherapy had not responded to previous medical treatment, had evidence of complications or intractability of ulcer and were considered possible candidates for operation. Several had severe cardiac disease contraindicating operation. One patient became cyanotic on the operating table before surgery and operation was cancelled. Cobalt-60 teletherapy was not used in patients having simple uncomplicated ulcers or having a first attack of peptic ulcer.

Of our 34 patients, 28 had duodenal ulcer, four had marginal ulcer, one had gastric ulcer, and one had severe hyperacidity syndrome but no demonstrable ulcer. The average duration of ulcer distress was 11.3 years in the 28 patients having duodenal ulcer. Of these 28 patients, all had had repeated recurrences of ulcer, ten had hemorrhage, six had complications of obstruction, and one had perforation. The average duration of ulcer distress was 11 months in the four patients having marginal ulcer. Two had hemorrhage from the ulcer and all had pain. Two of the four patients

had had two operations each for ulcers. The patient with gastric ulcer had a 15-year history of previous duodenal ulcer. The patient with severe hyperacidity syndrome but no demonstrable ulcer, had been advised by another gastroenterologist to undergo gastric resection because of the severity of the symptoms.

The average length of follow-up in patients with duodenal ulcer was six months (range from 2 months to 2 years). The average duration of follow-up in the other six patients was 11 months. This follow-up is too short for the findings to serve as a basis for final conclusions concerning results of treatment. With a longer follow-up one might expect a return of hyperacidity in more of the patients and a higher incidence of recurrence of peptic ulcer and its complications.

TOLERATION OF THERAPY

As mentioned previously, the 34 patients were given an average depth dose of 2000 roentgen units each, with the cobalt-60 teletherapy unit. Pretreatment and post-treatment white cell counts and hemoglobin determinations showed no significant change. No skin reactions of any kind were observed in any of the patients. Six of the 34 patients complained of nausea and two patients vomited. Cobalt-60 teletherapy was better tolerated than was irradiation with a 250-kv. roentgen ray machine: the same dose delivered with a 250-kv. machine results in some erythema and tanning of the skin and in nausea and vomiting in a higher percentage of patients.

Transient mild jaundice occurred in one patient who had severe cirrhosis with esophageal varices in addition to his peptic ulcer. It was possible that the irradiation resulted in some necrosis of liver cells and jaundice since the patient had very serious impairment of his liver function before irradiation.

RESULTS

Gastric Secretory Studies

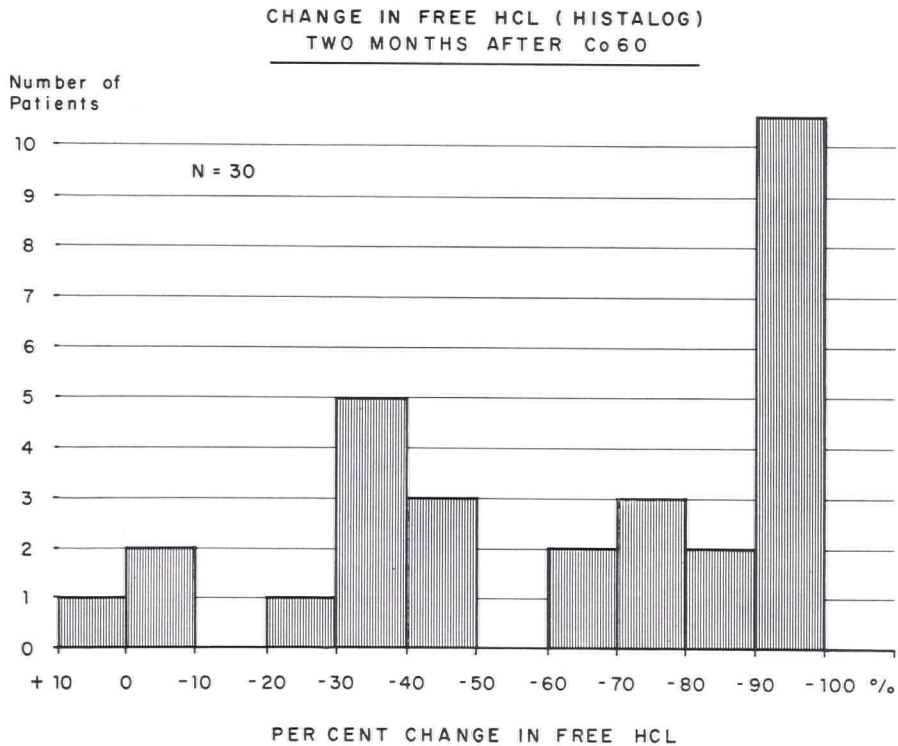
Gastric analysis gives us an objective measure of the effect of irradiation. The possible beneficial effect must be secondary to a decrease in gastric acidity. Gastric analyses with Histalog as a stimulant were obtained before and after irradiation. Histalog, which has been found to be comparable to histamine,¹¹ was used as a stimulant to obtain a maximum gastric secretory response.

Progress gastric secretory studies were obtained in 2 months in 30 patients. Gastric analyses obtained two months after cobalt-60 teletherapy showed an acidity in seven (23%) of the 30 patients. Eleven (37%) had a reduction in gastric acidity of 90% or more. Eighteen (60%) had a reduction of gastric acid secretion of 60% or more. It should also be noted that 18 (60%) of the patients developed a fasting anacidity which is seldom present in patients with duodenal ulcer.

Six months after treatment with cobalt-60, the depression of gastric acid secretion was not so great. Only 1 in 15 patients had an anacidity to Histalog. Decrease in acidity was less marked in 8 of 15 patients as compared with that two months after irradiation. Consequently, with time there may be a gradual return of gastric acid secretion to pretreatment levels.

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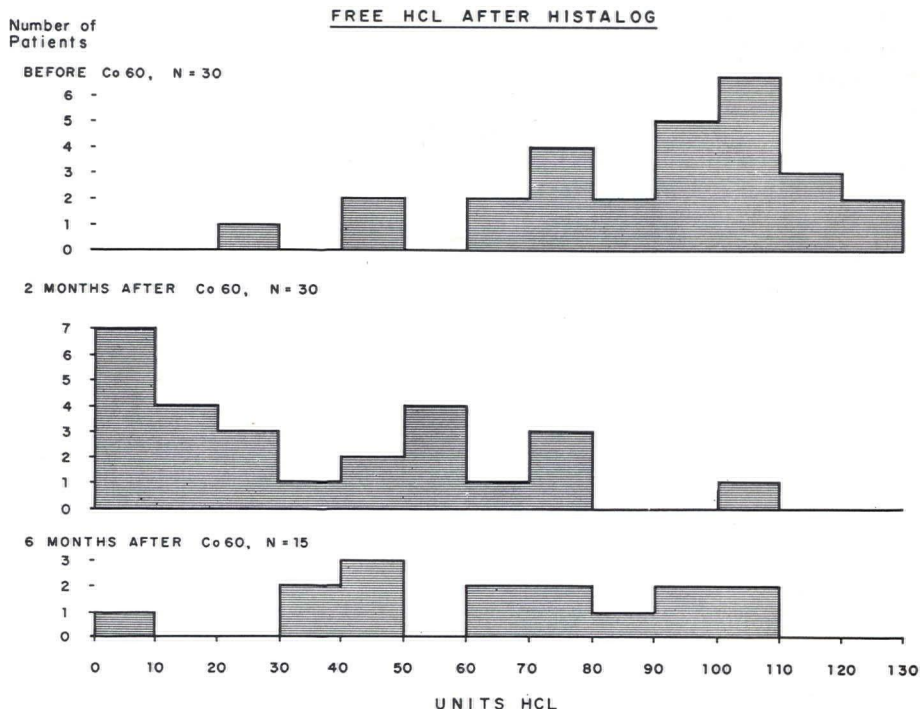
In Figure 1, the per cent change in free hydrochloric acid secretion after stimulation with Histalog two months after irradiation is compared with preirradiation levels. Three patients had no appreciable change; nine patients had a decrease of 20 to 50%; and eighteen patients had a decrease of 60% or more.



In Figure 2 are shown the concentrations of free hydrochloric acid secretion before irradiation, two months after irradiation, and six months after irradiation. In the top graph is a distribution before cobalt-60 therapy. Note the large number of patients with secretion of 90 or more units of free hydrochloric acid. The second curve is a distribution two months after cobalt-60 therapy. Note the marked decrease in acid concentration. The bottom curve shows the acid secretion six months after irradiation. There is a shift of the distribution to levels higher than those found two months postirradiation but still not so high as those found preirradiation. Despite that these studies show that irradiation with cobalt-60 appreciably decreases gastric acid secretion. Such a decrease may be temporary only, at least in some patients.

Symptomatic Response

It is difficult to evaluate symptomatic response of patients having peptic ulcer to any type of therapy. Ulcer is characterized by spontaneous remissions and exacerbations. Nonetheless, the long histories of ulcer in the group, the number of complications and the lack of response to previous medical, and in four cases surgical, treatment are in some measure a control.



Of the 28 patients with duodenal ulcer, 27 had prompt relief of symptoms. One patient had recurrence of symptoms in 12 months. Another patient had an acute perforation in three and one-half months; however, the depression of gastric acidity after cobalt-60 therapy was not great in this patient. Before the perforation occurred, he was entirely asymptomatic and roentgen studies of the stomach showed that the ulcer crater had healed. At operation he was found to have a perforation of a new acute ulcer rather than of the old ulcer.

All of the patients with marginal ulcer obtained symptomatic relief after cobalt-60 therapy, but one year after treatment one patient had a recurrence with a further episode of bleeding. Gastric acidity at the time of the recurrence showed that the hyperacidity had returned.

The patient with gastric ulcer had prompt relief of symptoms; there has been no recurrence during the past 12 months. The patient with the hyperacidity syndrome obtained only partial relief after irradiation.

Roentgen Response

Initial roentgen studies of the stomach demonstrated an ulcer crater in each of the 28 patients with duodenal ulcer. We did not give cobalt-60 therapy unless the patient had a definite ulcer that was demonstrated on roentgenograms. Progress roentgen examinations of the stomach two months after cobalt-60 therapy were obtained in 24 of the 28 patients with duodenal ulcer. The ulcer crater had dis-

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appeared in all 24 of the patients, and in addition six patients who showed evidence of obstruction prior to cobalt-60 therapy had no evidence of obstruction on the progress roentgenograms.

In the four patients with marginal ulcer, progress roentgen studies showed the ulcer to have healed in three patients but to have recurred in one.

In the patient with gastric ulcer, progress roentgenograms two months after cobalt-60 therapy showed that the ulcer was healed. For one year since that time, progress roentgen studies at three-month intervals have shown no recurrence of the ulcer.

Failures in Treatment

Failures in treatment occasionally can be more informative than successes. Since the purpose of cobalt-60 teletherapy is to decrease gastric acid secretion, if such a reduction does not occur the case must be listed as a failure. Similarly, if the gastric secretion returns to pre-treatment levels, the case also must be listed as a failure.

Of the 34 patients treated with cobalt-60 teletherapy, nine must be designated as failing to respond satisfactorily. Of these nine failures, six remained asymptomatic but either had a persistence of hyperacidity by gastric analysis or had a recurrence of hyperacidity after an initial depression.

Only three patients were clinical failures having recurrence of hyperacidity associated with recurrence of ulcer. The patient with a duodenal ulcer who developed an acute perforation three and one-half months after therapy already has been discussed. The patient with marginal ulcer who developed recurrence of pain and an episode of gastrointestinal bleeding one year after irradiation has been given a second course of cobalt-60 teletherapy and further medical treatment. Before the first course of teletherapy this patient had undergone two operations for peptic ulcer, a gastric resection for duodenal ulcer followed in six months by a vagotomy for marginal ulcer. The third patient who was a symptomatic failure is a patient with duodenal ulcer with obstruction who had recurrence of symptoms and obstruction one year after irradiation. Because of severe coronary heart disease, this patient was not operated upon but was given a second course of irradiation and continued medical treatment.

Even though the follow-up period is short (average six months), the small number of patients (three) who were symptomatic failures is encouraging. The long history of ulcer in this group of patients, the number of complications and the severity of the patient's distress make the good response of the remaining 31 patients more significant than if the patients had early uncomplicated peptic ulcer. For example, one of our patients had received 50 to 100 mg. of meperidine hydrochloride, three to four times daily, for relief of ulcer symptoms for three years prior to treatment. He has now been followed for ten months since irradiation with cobalt-60 and has not required a single injection of meperidine. A good response to treatment in such a patient with so-called surgical ulcer is more significant than a good response in a patient with an early simple peptic ulcer.

SUMMARY

Cobalt-60 teletherapy was given to 34 patients with complicated peptic ulcer as a supplement to medical treatment. These patients had not previously responded to medical treatment and had an average duration of ulcer distress of 11.3 years.

Therapy was well tolerated; there were minimal reactions with no skin changes or tanning.

In all but three of the 34 patients, gastric acidity was decreased by cobalt-60 therapy. There was a gradual return of acidity in some patients to pretreatment levels in six to twelve months. The initial symptomatic and roentgen response was good in all patients. There was a recurrence of symptoms, hyperacidity, and ulcer in three of the patients, two of whom have been given a second course of irradiation with cobalt-60.

We do not advise irradiation for the simple uncomplicated peptic ulcer that should respond to conventional medical treatment. Irradiation with cobalt-60 may be indicated in many patients with complicated or "surgical" ulcer or with repeated recurrences of peptic ulcer. Surgical treatment may be avoided in some of these patients with complicated peptic ulcer by the combined use of cobalt-60 irradiation and intensive conventional medical therapy.

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