# *Therapeutic Trial of Silicone In Peptic Ulcer*

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THE FACT that no known therapeutic regimen will prevent recurrence of peptic ulcer or will heal peptic ulcers in all patients has led to the search for methods of therapy other than those directed at reduction or control of acidity. The possibility that coating substances might effectively prevent acid peptic digestion of the mucosa has been considered, but up to the present time no effective "coating" substance is available. Investigations initially carried out in animals showed that silicone, which is such a "coating" substance, would effectively prevent ulcers in pylorus-ligated rats[1] suggested to us the possible use of silicone in peptic ulcer in man. Subsequent studies showed that dogs receiving silicone by stomach tube seemed to be protected against the formation of histamine-induced ulcers. In addition, in dogs given silicone after ulcers had been produced by daily histamine administration, the histamine-induced ulcers healed even though histamine injections were continued.[2] In view of this we felt that we were justified in evaluating silicone in patients with peptic ulcers. A long-term, double-blind trial was designed to compare the effects of silicone with placebo therapy.

## EXPERIMENTAL DESIGN

Any patient of either sex and any age was admitted to the trial if he or she indicated willingness to attend regularly once a month for 6 to 12 months on the following medical indications:

1. A definite diagnosis of ulcer must have been made, either gastroscopically, radiologically, or on indisputable clinical grounds within the last 18 months.

2. No patient who had been symptom-free for over 4 months was admitted to the trial until, and unless, symptoms developed.

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3. The members of the Gastroenterology Clinic had complete control of the patient's therapy throughout the trial or the patient was dropped from evaluation.

Both outpatients (chronic active ulcer) and inpatients (acute active ulcer) were admitted to the trial. Any patient admitted to the hospital for medical treatment of the ulcer was seen daily on ward rounds, and all outpatients were seen at least once every month and many of them at more frequent intervals, depending on the state of the patient's symptoms.

A 30 per cent silicone emulsion (Dow-Corning Corporation),* suitably flavored, and a physically similar preparation containing 20 per cent aluminum hydroxide were furnished by Eli Lilly and Company. It was found necessary to add the aluminum hydroxide to the placebo medication in order to provide a texture similar to that of the silicone emulsion. The patients getting the placebo preparation received the equivalent of 1 to 3 cc. of aluminum hydroxide gel six times daily. We felt that this amount was well below the optimum therapeutic one. Each patient, on admission to the trial, received a number according to the random allocation of numbers previously made. The number was checked by the pharmacist against the master list, a copy of which was held by the chief pharmacist so that the patient received the same mixture throughout the trial. The bottles were labeled with the patient's name and number only, so that at no time did the physician in charge of the case know what medication the patient was receiving. All patients were advised to eat three meals daily with interval feedings and were told to take Bellarbital, (containing phenobarbital 15 mg. and belladonna 16 mg.), one tablet 4 times daily. No other long-term or chronic medications were utilized in this study other than either the placebo or the silicone emulsion.

The results were assessed on the following: (1) Relief of acute symptoms while in the hospital; (2) prevention of recurrence of pain; and (3) prevention of complications such as hemorrhage, perforation, and/or the necessity for operation. The first objective, the relief of acute symptoms, was established by day-to-day interview of the ulcer patients in the hospital, noting the patients' description of pain in the previous 24 hours, the number of tablets of antacid needed by the patient, and complications occurring in

*The silicone was an antifoam, described in the early experiments[1, 2] as XEC 151, and as shown in later experiments as 240-41-101.

the hospital. The prevention of recurrences and complications was the major object of the regular monthly observations and interviews in the outpatient department, where the following points were noted: (1) patient's weight; (2) amount of pain complained of by the patient; (3) complications, if any; and (4) status of bowel habits (the effects of silicone).

## RESULTS

Table 1 summarizes the over-all results in patients treated with silicone and placebo, respectively, at 3-month intervals up to 1 year after starting treatment. Of the placebo group, 27 of 32 were "cured" at 3 months and 23 of 28 at 6 months (85 per cent and 82 per cent, respectively).

These high figures for improvement are the most important because ulcer patients seen at the University Hospital are, in general, those who have been intractable on previous treatment. On questioning, practically all of these patients stated that they had taken Amphojel in the past, and had either not had satisfactory response to it or had become refractory to it. In spite of this and because they realized that they were being tried on a "new drug," 82 per cent of these patients previously refractory to Amphojel therapy were improved at the end of 6 months when given highly diluted Amphojel. In other words, it would seem that the therapeutic effects of the patient's emotional response to a "new drug" therapy was extremely great. It would seem on this basis that giving an ulcer patient anything that is not harmful to the patient could result in improvement in at least 80 per cent if followed for

**TABLE 1. Results of Silicone and Placebo Treatment in Patients with Duodenal Ulcer**

| | 3 Months | | 6 Months | | 9 Months | | 12 Months | |
|---|---|---|---|---|---|---|---|---|
| *Placebo:* | S | F | S | F | S | F | S | F |
| Males | 24 | 5 | 20 | 5 | 16 | 8 | 10 | 13 |
| Females | 3 | 0 | 3 | 0 | 2 | 1 | 1 | 1 |
| TOTAL | 27 | 5 | 23 | 5 | 18 | 9 | 11 | 14 |
| *Silicone:* | S | F | S | F | S | F | S | F |
| Males | 20 | 10 | 16 | 12 | 13 | 14 | 10 | 16 |
| Females | 3 | 1 | 1 | 3 | 1 | 3 | 1 | 3 |
| TOTAL | 23 | 11 | 17 | 15 | 14 | 17 | 11 | 19 |

S = Success of therapy to date.
F = Failure of therapy to date.

only 6 months. A smaller proportion, 23 of 34 (68 per cent) patients on silicone treatment, were improved at the end of 3 months. It is interesting to note that as time went by at 6 months, 9 months, and finally at 12 months, the placebo and silicone groups tend to become more and more similar, so that at the end of one year only 11 of 25 patients still being followed in the placebo group, or 44 per cent, were improved, and 11 of 30, or 37 per cent, were improved in the silicone group.

## DISCUSSION

It is obvious that the silicone used in this study had no intrinsic therapeutic effectiveness either in the relief of acute symptoms or in the prevention of recurrences or complications of peptic ulcer disease. In fact, the over-all relapse rate was greater over the whole study (see Tables 1 and 2) ($\chi^2 = 20.116$; $df = 9$; $p < .02$). The failure of the silicone to remain effective prompted a repeat check on the effectiveness in experimental ulceration. As it turned out, the study was actually conducted with two ineffective drugs, 240-41-101, (the silicone) and 240-41-86 (the placebo).[3] It thus was in effect a study of the natural history of chronic peptic ulceration under close observation with its inevitable psychosomatic overtones.

The importance of an "emotional cofactor" in the treatment of peptic ulcer is brought out strikingly by the fact that at 3 months 77 per cent of the patients in both groups had been relieved of their acute symptoms and had not had recurrences and, at the end of 1 year, 40 per cent of patients were still relieved of their symptoms and had not had significant recurrences. Besides emphasizing the significance of the emotional cofactors in the therapy of peptic

**TABLE 2. 4 × 4 Contingency Table Constructed from Data in Table 1 (Males and Females Combined), Showing Significant[a] Differences Between Treatments[4]**

| | 3 Months | 6 Months | 9 Months | 12 Months | Total |
|---|---|---|---|---|---|
| Placebo | | | | | |
| Successful | 1.240 | .517 | .075 | 2.848 | 4.680 |
| Failed | 1.847 | 1.312 | .125 | 5.389 | 8.673 |
| Silicone | | | | | |
| Successful | 1.453 | .030 | .205 | 1.066 | 2.754 |
| Failed | 2.176 | .023 | .266 | 1.544 | 4.000 |
| TOTAL | 6.716 | 1.882 | .671 | 10.847 | 20.116 |

[a] $df = 9$; $\chi^2 = 20.116$; $p < .02$.

ulcer, these results underscore the absolute necessity of carrying out double-blind studies of adequate duration before any conclusions as to the therapeutic efficacy of any drug in the treatment of peptic ulcer can be evaluated.

## SUMMARY and CONCLUSION

In a controlled double-blind trial of the therapeutic effectiveness of silicone in patients with duodenal ulcer, the silicone tested was shown to be slightly less effective than placebo medication. The relatively good early response of chronically recurring ulcer disease appeared to be due to the emotional impact of "a new treatment of ulcers."

## REFERENCES

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