THE JOURNAL OF

The American Geriatrics Society

Official Journal of the American Geriatrics Society

VOLUME I | *May, 1953* | NUMBER 5

EVALUATION OF PRESENT DAY TREATMENT OF PEPTIC ULCER

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The treatment of peptic ulcer is an ever increasing problem to the internist and surgeon alike. Those who attempt to treat the ulcer patient conscientiously are daily confused by the multiplicity of articles and conflicting results found in the literature today. There are many advocates of a strict antacid and dietary regimen and almost as many others claim that antacids and diet are valueless. Many substances have been proposed as sure cures for the peptic ulcer patient, only to have this claim upset by reports indicating that placebos are just as effective.

It is extremely difficult for the average busy practitioner to weigh the evidence and sift the facts in an attempt to determine what actually constitutes the most adequate present day method of therapy. It is the purpose of this paper to summarize and clarify the modern treatment of peptic ulcer.

In 1828 Abercrombie (1) first introduced the use of milk, farinaceous foods and lime water in the treatment of this disease. Johnson (2) just three years later introduced the use of soda, magnesia and chalk. In 1835 Cruveilhier (3) emphasized the use of good dietary hygiene and in 1872 Fox (4) stressed the importance of rest. Since that time the treatment of peptic ulcer has been modified very little. The basis for the modern day treatment of peptic ulcer was established by the year 1872; only antispasmodics, sedatives, and psychotherapy have been added.

The etiology of peptic ulcer remains almost as obscure as it was in 1872. No single etiologic factor has been found but many factors have been presented as playing a role in the causation of this disease. Decreased tissue resistance secondary to the loss of the normal mucous barrier has been advanced by some authors as the basic cause of peptic ulceration. No good evidence has appeared to show a decrease in mucin content and the use of gastric mucin in the treatment of peptic ulcer has been discouraging. Other investigators have postulated the presence of gastric atrophy as the cause of decreased tissue resistance and

Received for publication February 12, 1953.

ulcer formation. This notion has been discarded, since direct examination of the stomach by means of the gastroscope has failed to show the presence of either chronic gastritis or gastric atrophy in the majority of patients with either duodenal or gastric ulcer. The old concept that either vascular thrombosis or embolism produces an infarction has long been discarded. Other theories as to etiology have included infection, allergy, nutritional deficiency and heredity. None of these theories has withstood the test of time and in no instance has unimpeachable evidence been presented to substantiate these claims. Other factors, such as increased pepsin content, decreased alkaline secretions (pancreatic juice or bile) or decreased secretion of alkaline juice by Brunner's glands, have been incriminated. Studies by Ihre (5), Comfort and Osterberg (6), and Boyden and Berman (7) have failed to demonstrate significant alteration in the rate of secretion of these substances in patients with peptic ulcer.

Intensive survey of the literature indicates that the only consistent finding in the presence of benign peptic ulcer is free hydrochloric acid. Ulcers in the duodenal bulb are usually accompanied by hypersecretion, whereas gastric ulcers seem to be more consistently associated with a normal or low gastric acidity. There seems to be a better case for the presence of decreased tissue resistance in gastric ulcer than in duodenal ulcer. Exactly what this decreased tissue resistance can be attributed to is not, as yet, known. The role of free hydrochloric acid in the production of peptic ulcer is supported by overwhelming experimental and clinical evidence. Experimentally it has been shown that gastric juice containing free hydrochloric acid can digest all living tissues. Ulcers can be regularly produced in animals by stimulating acid secretion by various means. Clinically it has long been known that peptic ulcers develop only in those areas of the gastrointestinal tract exposed to acid gastric juice. These areas include the lower esophagus, stomach, duodenum (first portion), and the jejunum in patients with gastroenterostomies. Ulcers may occur in a Meckel's diverticulum if it contains acid-secreting gastric mucosa. There have been no proven cases of chronic benign peptic ulcer occurring in patients with persistent achlorhydria. Neither Sturgis (8) nor Washburn and Rozendaahl (9) have been able to find a case of benign peptic ulcer in patients with pernicious anemia.

It must, therefore, be concluded that peptic ulcer develops only in patients with parietal cells capable of secreting free hydrochloric acid. The fact that hypersecretion is not found in all patients with peptic ulcer suggests an additional factor, such as decreased tissue resistance, playing a part in the formation of the ulcer. Since the nature of this decreased resistance is not definitely established, the modern treatment of peptic ulcer must be directed at the control of acidity.

The source of hydrochloric acid, the parietal cell, is susceptible to stimulation by many different means. Unfortunately these cells are not as susceptible to depression as they are to excitation. There are, however, many methods available for the neutralization of the acid after it has been produced. That there is no consistent and sure method for this neutralization is manifested by the multiplicty of antacids and dietary regimens prescribed for this purpose. We shall

consider these various methods for controlling free hydrochloric acid and from this arrive at an acceptable program for the treatment of peptic ulcer.

For the past few decades emotional factors have been known to enter into the picture of peptic ulcer. In 1932 Draper and Touraine (10), writing on the man-environment unit and peptic ulcer, felt that "excessive anxiety from the threat of an excessive feminine component in the personalities of men plays a major role in the etiology of peptic ulcer." Since that time various investigators, including Alexander (11), Mittelman and Wolff (12), Sasz *et al.* (13), and others, have reported on the role of emotions in the ulcer patient. That these patients have, in general, an ambitious conscientious type of personality is well recognized by the medical profession in general. Objective evidence of the role of emotions in controlling the gastric secretory rate and motility can be obtained by direct measurements. Since the experiments of Pavlov, numerous investigations have confirmed his contention that gastric secretion in man is predominantly under neural control. That this control is mediated primarily through the autonomic nervous system is borne out by the increased secretion following vagal stimulation. Likewise, decreased secretion has been noted following sympathetic stimulation. The autonomic nervous system activity seems to be concerned only with the regulation of hypersecretory states, and has little to do with basal and nocturnal secretion. Vagal denervation, therefore, usually results in a reduction of the hyperacidity but has relatively little affect on the basal and nocturnal secretory rate. That emotional states play some role cannot be denied. That the emotional-conflict state is the cause of ulcer production is open to serious question. Although it is true that there seems to be a general personality pattern in ulcer patients, there are a large number who fall outside this pattern. It should also be remembered that, although hypersecretion can be induced by certain emotional states, this hypersecretion is of relatively short duration, whereas in most ulcer patients the hypersecretion continues and is most noticeable in the basal and nocturnal secretory rates.

Psychotherapy

There is no proof that psychotherapy of itself, produces material benefit for any substantial period of time. Stine and Ivy (14) have recently reviewed the results of psychiatric therapy in ulcer patients. After sending questionnaires to all members of the American Psychoanalytic Association they were able to collect only 7 cases suitable for follow-up. Of these cases, 2 were reported to be unimproved and 5 improved. The 5 improved patients had been followed for periods of six months to eight years. Three of these were said to have recurrent episodes of substernal and epigastric distress ascribed to "heart-burn," 1 had recurrent episodes of bleeding, and 1 had recurrence of epigastric pain which was felt to be due to ulcer activity. Keeping in mind that ulcers have a proclivity for healing themselves, it would seem that these results cannot be interpreted as being satisfactory. Until further proof of the value of intensive psychotherapy is offered it would seem best that these patients be treated by the internist or family physician. "Superficial" psychotherapy consisting of an understanding

and sympathetic attitude plus a liberal amount of reassurance should always be a part of medical therapy. These patients need both physical and mental rest and we frequently employ phenobarbital in doses of 16 to 32 milligrams three times a day along with "superficial" psychotherapy in an attempt to afford the patient this necessary relaxation.

From the purely medical aspect of ulcer therapy there are three things of importance in the control of acidity and the ulcer. These are the diet, and the employment of antacids and antispasmodics.

Diet

Lenhartz (15) first utilized the multiple-feeding technique in the treatment of the ulcer patient. This rapidly replaced Leube's starvation regimen. The excellent results of Lenhartz' multiple-feeding schedule was confirmed by subsequent investigators. Meulengracht (16), although often given credit for originating this method, merely re-awakened interest in Lenhartz' original work. Other more specialized dietary methods have been introduced from time to time. The most widely recognized regimens are those of Bertram Sippy (17) and Asher Winkelstein (18). The Sippy regimen, consisting of milk and cream with Sippy powders (magnesium oxide, calcium carbonate, and sodium bicarbonate), has been modified greatly and is adhered to less and less. There are many reasons for the modification of Sippy's regimen. It was nutritionally inadequate during the first three weeks, being especially low in vitamin C, and it did not result in as effective a control of gastric acidity as originally thought. The strictness of the diet was disliked by many patients and it did not seem to influence greatly the incidence of ulcer recurrence. Asher Winkelstein was concerned about the number of ulcer patients suffering from nocturnal pain. Since ulcer patients generally have a high rate of nocturnal acid secretion, Winkelstein modified his original intragastric drip method. Under his new regimen he allowed the patients to have three liberal bland meals per day and added sedatives, antacids, and atropine at various intervals during the daytime. In addition he ran a constant milk drip through a gastric tube between each meal and throughout the night. Although this strenuous therapy may be necessary in exceptional cases, it has been our experience that the relief of acute episodes can be just as effectively maintained by less strenuous measures. The problem of immediate relief has not been of great concern. The greatest problem has presented itself in the question of long-term treatment and the prevention of recurrences. Winkelstein's regimen has not solved this matter and it is our belief that these patients do better over a long period of time when there is as little interference as possible with the normal diet. To this end we have routinely employed a modified Meulengracht diet (Table 1).

This diet avoids the unpleasantness of intubation, as is required in the Winkelstein regimen. It affords the patient adequate calories and vitamins, and has been shown to be just as effective in controlling acidity, relieving pain, and healing the ulcer (19).

TABLE 1

Beverage
Milk, milk beverage, coffee substitute.

Bread
Bread (day-old) or toast (white or rye), soda crackers, zwieback.

Cereal
Cornmeal, farina, hominy grits, oatmeal, prepared corn cereal, prepared rice cereal rice, fine whole wheat cereal, other wheat cereal, strained.

Dessert
Bread pudding, cake (plain), cookies (plain), cornstarch pudding, custard, fruit puree whip, gelatin dessert, ice cream or ice (plain or with fruit puree), junket, rice pudding, tapioca pudding.

Fat
Butter or vegetable shortening.

Fruit
Any fruit puree or juice, fresh banana, canned Royal Anne and Bing cherries. Peeled and cooked: apples, apricots, peaches, pears, plums, prunes, rhubarb.

Meat or substitute
Beef, lamb, pork, veal: roast, boiled, broiled, baked.
Cheese: American (finely divided and in combination with other foods), cottage, cream.
Chicken: stewed, creamed, broiled, baked.
Eggs: coddled, poached, soft cooked, hard boiled, creamed, scrambled in a double boiler.
Fish: fresh, canned salmon or tuna: boiled, broiled, baked, creamed.
Liver: boiled, baked, creamed.
Oysters or sweetbreads: stewed, creamed, escalloped.

Potato or alternate
Prepared in any way except fried: macaroni, noodles, rice, spaghetti, Irish or sweet potatoes.

Seasoning
Salt.

Soup
Creamed soup made from allowed vegetables.

Sweets
Sugar, syrup, jelly, and chocolate.

Vegetables
Puree: string beans, beets, corn, peas, spinach, tomato.
Cooked tender: asparagus tips, carrots, egg plant, pumpkin, squash.

Avoid
1. Highly seasoned foods and sauces, catsup, horse radish, mustards, pickles and condiments.
2. Cabbage, onions, peppers, radishes, and turnips.
3. Rare meat, meat soup, broth and gravy.
4. Corned beef, frankfurters, sausage, smoked meat and fish, or any prepared nuts.
5. Fried food, hot bread and pastry.
6. Nuts.
7. Very hot and very cold food, unless eaten slowly.
8. Overeating.

Sample Menu

Breakfast	*Noon*	*Evening*
Orange juice	Creamed chicken	Strained cream of tomato soup
Cream of wheat	Mashed potatoes	Scrambled eggs
Toast	Green bean puree	Baked potato
Butter	Bread	Pea puree
Beverage	Butter	Bread
Cream	Lemon cream pudding with meringue	Butter
Sugar, if desired	Milk	Applesauce
		Milk

Midmorning, midafternoon and evening: Milk or milk beverage, crackers, cookies, bread or cereal.

Antacid therapy

As far as antacid therapy is concerned, we have found magnesium trisilicate and calcium carbonate to be as effective, or in many instances, more effective than amphojel®, phosphojel®, sodium bicarbonate or any of the many mixtures placed on the market under various commercial names. Magnesium trisilicate was first introduced by Mutch (20) in 1936. It has a gradual and prolonged action and reacts with acid by a dual mechanism. It acts as an absorbent and, in addition, reacts chemically with acid thus:

$$Mg_2SiO_3 \cdot 2H_2O + 4HCl \rightarrow 2MgCl_2 + SiO + 4H_2O$$

The effectiveness with which it reacts has been demonstrated repeatedly both *in vitro* and *in vivo*. Magnesium trisilicate is nontoxic and without serious side effects. We have never seen diarrhea of any serious degree develop. Since the magnesium ion, however, may tend to cause diarrhea in some patients it may be feasible to alternate this drug with calcium carbonate, an equally effective antacid. It is our practice to use either one, in dosages of 1 to 2 grams six times daily.

Antispasmodics

The use of antispasmodics has been incorporated into the routine therapy of peptic ulcer. We usually employ tincture of belladonna in a dosage of 15 to 30 drops four times daily. It has been our experience that this preparation is just as effective as many of the newer synthetic antispasmodics. If methantheline (Banthine®) bromide is chosen, a word of warning regarding its use in the presence of partial obstruction should be issued. We have seen occasional cases seemingly become more and more obstructed during the use of Banthine. The primary action of this drug is to cause a decrease in gastric motility and tone. In the face of partial obstruction this loss of tone may result in serious gastric distention and retention. These observations have been repeatedly made in the literature. The initial encouraging reports regarding the use of Banthine are being overshadowed by less enthusiastic or even adverse results. Of great interest is the recent report of Liebowitz *et al.* (21) in which they demonstrated the rapid development of refractoriness to the use of Banthine. During their investiga-

tions a dose of as much as 1.8 grams was given daily without maintaining depressant effects on gastric motility and secretory rate.

The blocking agents, hexamethonium salts and tetraethyl ammonium chloride and bromide, have been too variable in their effects on acid and too constant in side effects, to warrant their inclusion in the treatment of peptic ulcer. Postganglionic depressing agents such as dibutoline have been found to be less effective than either atropine or Banthine.

Miscellaneous

There have been many substances advanced as ulcer cures or as substitutes for the standard ulcer therapy of which we have written. Of these, gastric mucin has already been mentioned. There has been no evidence to show that it materially benefits the ulcer patient. Enterogastrone, a substance liberated by the intestinal mucosa in response to the ingestion of fats and inhibiting motor and secretory activity of the stomach, has been claimed to be effective both in animals and in man in preventing and healing peptic ulcers. More recent studies by Grossman (22), Pollard (23), Wollum (24), and other investigators have shown this hormone to be ineffective. There has appeared no proof regarding the effectiveness of other similar extracts, *e.g.*, preparations of hog stomachs and duodenum (mucosal and submucosal), desiccated and defatted raw whole mammalian duodenum (Viodenum®) or unspecified protein-free preparations of stomach or small intestine (Robuden®). Detergents have not been shown to be effective in man. The use of the newer cation exchange resins (Resinat®) have not been of material benefit thus far in the treatment of peptic ulcer. Martin and Wilkinson (25) have emphasized the importance of mesh or particle size in the use of resins, and further investigation along these lines may yet produce a more effective drug in the therapy of peptic ulcer. Combinations of various drugs (Carmethose, Mucotin, Resmicon, Chloresium powder) have given unspectacular results. X-ray therapy has been used in the treatment of peptic ulcer. Ricketts, Palmer, Kirsner, and Hamann (26) have shown that the percentage of patients whose ulcers heal, when x-ray therapy is given to the corpus and fundus of the stomach, is increased from 70 per cent when medical therapy alone is used, to 94 per cent when appropriate x-radiation therapy is added to the medical regimen.

SUMMARY

In the past twenty years many new methods have been proposed in the treatment of peptic ulcer. Critical evaluation of the results of these "advances" leads to the conclusion that peptic ulcer is still best treated by the simplest and time-tested procedures. These include the physician's genuine interest in the patient's problems, the enforcement of physical and mental rest with so-called "superficial psychotherapy," liberal amounts of reassurance, sedation as necessary, the use of a liberal bland diet, tincture of belladonna, and an antacid such as calcium carbonate or magnesium trisilicate. Although many false starts have been made along new lines of therapy during the past few decades, there is hope that some specific form of treatment may result from continued investigation in this field.

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