Antacids and Ulcer Healing
A Review of the Evidence

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Summary
There have been a number of controlled trials of antacids in the treatment of patients with peptic ulcer disease. As a general rule the size of studies has been small and there have been difficulties ensuring adequate blinding, because of the formulation and taste of the antacids. Despite these difficulties, antacids appear to be effective ulcer healing agents with efficacies resembling those of other antiulcer drugs. Definite dose relationships are unclear but high doses of buffering capacity over 200 mmol/day appear unnecessary and are associated with increasingly frequent adverse effects. Low dose maintenance treatment is effective at limiting duodenal ulcer relapse.

Antacids are generally considered inexpensive and are available 'over the counter' in pharmacies and supermarkets throughout the world. Their traditional role has been to provide symptom relief in flatulent dyspepsia. The enormous use of these drugs suggests that they provide some benefit, although proof of ulcer healing has been sought only in the last decade. This article summarises those trials which have attempted to measure this therapeutic effect.

Antacids neutralise gastric acid, thus raising intragastric pH; however, this obvious action may not be the only mechanism involved in their symptomatic and healing roles. Most antacids include magnesium or aluminium hydroxide alone or in combination with other salts of calcium and sod-
ium bicarbonate. The duration of antacid residence in the stomach (Grossman 1956) and the interaction of its constituents determine the buffering capacity (Littman 1967). Much significance is placed on the in vitro potency of different antacids, which is measured by adding hydrochloric acid to an antacid/water mixture until the pH reaches 3 (Fordtran et al. 1973). Although league tables have been produced showing which antacids are most ‘potent’ (according to this criteria) [Richardson & Peterson 1988], trials suggest that this may not be particularly relevant (see also section 5).

Alternative mechanisms of action of antacids in ulcer treatment have been suggested, the most prominent being stimulation of endogenous prostaglandins (PGs). Two groups have shown that aluminium hydroxide increases rat gastric PGE2 (Szelenyi et al. 1983; Tarnawski et al. 1984). Furthermore, mucosal protection by antacids – i.e. a reduction in the ulceration caused by various injurious agents – occurs even when aspirin, which inhibits endogenous PG synthesis, is given, and thus endogenous PG formation cannot be the only explanation for this effect. The relationship of any such effects to ulcer healing (rather than prevention) is debatable.

1. Clinical Trials – The Problems

Antacids are usually considered as an entity, and the possibility that their different constituents might be more or less therapeutically important is not often considered. In some trials the actual formulation is not published, and in many the in vitro buffering effect of the antacid is either omitted or calculated by differing means. It is therefore difficult to state categorically that the buffering capacity of antacids does or does not define therapeutic efficacy.

In most peptic ulcer trials, other agents or antacids of various types have been given for symptomatic relief. As a consequence, in many of these trials it has not been possible to determine exactly how much antacid has been used. Symptomatic use obviously increases the tested ‘dose’ in terms of buffering or any other putative effect. Thus, conclusions derived from the dosage of the regularly scheduled antacid under examination may be misleading.

The most prominent problem in the antacid trials reviewed continues to be statistical power. In some studies too many comparison groups have been used, and in all, the numbers participating have been small. Blinding is difficult because of the taste and consistency of the active preparation. However, trials which have used endoscopy generally have been at least third party blinded. Treatments have also been randomly allocated in the majority of studies.

2. Symptom Relief from Antacids

Half the population in the United States use antacids for symptomatic relief of abdominal symptoms with perceived but poorly proven benefit (Graham et al. 1983). Controlled trials are difficult and suffer from the problems discussed above, but have generally failed to demonstrate that antacids are superior to placebo (Nyren et al. 1986). In one blinded trial, duodenal ulcer patients treated with either antacid liquid or placebo reported no significant additional pain relief from individual doses of antacid (Sturdevant et al. 1977). The improvement in symptoms resulting from antacid administration may approximate that achievable with placebo and cannot justify the present widespread use of antacids.

3. Duodenal Ulcer Healing

3.1 Comparisons with Placebo

Several controlled trials of very limited power show that antacids appear effective. In only one trial (Lam et al. 1979) was the difference between placebo healing and antacid healing nonsignificant, and in this study the confidence intervals were wide (table I). It seems reasonable to conclude that antacid treatment provides a benefit.