Correspondence

surface membrane as FMLP interacts with a surface receptor but PMA interacts with an intracellular receptor to activate protein kinase c which stimulates the oxidase enzyme.

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References


Reply

sir.—I wish to thank Dr Andrew Williams for his interesting and constructive comments on my recent paper.1 I agree with his opinion that the agent that inhibits neutrophil derived superoxide production also logically inhibits hydroxyl radical and hydrogen peroxide generation. In our experiments, SP mildly inhibited superoxide generation in the neutrophil system and also showed inhibitory trends in the xanthine-xanthine oxidase system, although the latter was insignificant. If SP had an SOD like activity, it will raise the level of hydrogen peroxide as we have previously reported.2 In this case, it is not unlikely that SP inhibits superoxide production slightly without apparently affecting hydrogen peroxide or hydroxyl radical levels, because the expected slight reduction in these levels induced by the mild suppression of superoxide production may be masked. Another possible explanation for this dissociation is a time gap between each assay being done, although this is less likely.

As mentioned in the paper, these agents seem to affect the oxygen metabolism of neutrophils with somewhat different and probably multiple modes of action, which makes the issue complicated.

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Teeth and benign oesophageal stricture

sir.—Maxton et al (Gut 1987; 28: 61–3) have found that benign oesophageal strictures occur more frequently in a group of edentulous patients attending for endoscopy than in a control group with normal dentition. They suggest that edentulous patients eat less solid food than controls and the lower oesophagus is therefore subject to less dilatation with a greater tendency to stricture.

An alternative explanation, however, is that the edentulous patients because of poor masticatory function, chew solid food less efficiently and therefore swallow larger boluses which are more likely to obstruct their strictures. In this way they have more symptoms of dysphagia and thus present earlier for dilatation. The authors have assessed neither the dietary intake or masticatory abilities of their patient groups, and whilst other papers have suggested that edentulous patients eat less solid food than 'normal', these factors have not been established in this study.

We would agree that patients with strictures should be urged to use dentures, not primarily to reduce stricture formation but to encourage better chewing and therefore less bolus impaction and dysphagia.

The discrepancy between severe symptomatic oesophagitis and the relatively symptom free patients who appear to develop stricture does not invalidate oesophagitis as a cause of stricture formation. It is possible that those patients who are symptom free have the most severe reflux oesophagitis precisely because they are unaware of their oesophageal damage and do not present until a stricture has formed.

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Reply

sir.—Drs Tait and McKinlay add another interesting suggestion for the cause of the increased prevalence of benign oesophageal strictures in the elderly with few or no natural teeth.

Because of their less efficient chewing, however, edentulous patients tend to choose softer, less solid food rather than eating larger poorly masticated boluses of more solid food. Thus, nuts and tough meat are rarely eaten by edentulous patients. We are
therefore more inclined to believe that smaller softer boluses are the problem rather than solely poor masticatory function although it remains possible that both factors may operate together.

We do not fully understand the last point in their letter. It seems unlikely that severe oesophagitis is associated with lesser symptoms.

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Essential fatty acids and peptic ulcer disease

Sir,—The recent proposal by Hollander and Tarnawski¹ on the relationship between essential fatty acids and peptic ulcer disease is not only interesting but also has some practical therapeutic implications. The criticisms made by Gibney² on this hypothesis and the rejoinder by Hollander and Tarnawski¹ made interesting reading. In this connection, we wish to add the following.

There are two families of essential fatty acids (EFAs), n-6 polyunsaturated fatty acids (PUFAs) derived from linoleic acid (LA), and the n-3 PUFAs derived from alpha-linolenic acid (ALA). Essential fatty acids cannot be synthesised by the body, but the body can desaturate and elongate EFAs provided by the diet. Linolenic acid is desaturated to form gamma-linolenic acid (GLA), which in turn is elongated to form dihomo-GLA (DGLA), the precursor of 1 series prostaglandins (PGs). Dihomo-gamma-linolenic acid can also be desaturated by delta-5-desaturase to arachidonic acid (AA), the precursor of 2 series PGs. Alpha-linolenic acid is desaturated and elongated by the same set of enzymes to give rise to eicosapentaenoic acid (EPA), the precursor of 3 series PGs. The activities of the desaturase enzymes are under hormonal and nutritional control.⁴

Prostaglandins administered exogenously,¹ or synthesised endogenously⁴ can prevent the formation of mucosal ulceration induced experimentally by aspirin, alcohol, bile acids, and even boiling water.⁵,⁷ In a recent review, Hawkey and Walt⁸ summarised the data available on PGs and peptic ulcer and pointed out that PG analogues did not appear to heal peptic ulcers better than would be predicted from their ability to inhibit acid secretion. In this connection, it is worth noting that the main thrust of the hypothesis by Hollander and Tarnawski is that EFAs are responsible for the marked decrease in the incidence and virulence of peptic ulcer disease as they can be rapidly converted to PGs by the gastroduodenal mucosa.¹³ We suggest here that this may only be part of the answer and propose that EFAs themselves may have the ability to enhance ulcer healing and possess cytoprotective properties.

Ethanol can inhibit delta-6-desaturase (d-6-d) activity which is necessary for the conversion of LA to GLA⁴ and chronic ethanol consumption induces decreased production of PGE₁.¹⁶ Similarly dexamethasone is not only a PG-synthesis inhibitor but also a blocker of d-6-d activity.¹¹ Thus, it can be suggested that both ethanol and steroids are ulcerogenic in nature as a result of their action on EFA and PG metabolism. In this context, it is interesting to note that Hollander and his colleagues¹² fifteen and others¹⁴ noted the protective effect of arachidonic acid and PGs against ethanol induced gastric mucosal damage which obviously bypass the blocking effect of alcohol on d-6-d activity. It would have been interesting to study the effect of LA in comparison with that of GLA or AA in preventing the ulcerogenic action of alcohol, steroids, and non-steroidal anti-inflammatory drugs.

In a recent study, Diel¹⁸ showed that GLA can protect rats from ethanol induced haemorrhagic gastric erosions. In a preliminary study, we observed that oral evening primrose oil (3.0 g/day) can heal ulcer. In a study of six patients, we found that duodenal ulcer (5 to 10 mm in size) had completely healed endoscopically within a period of four to six weeks with no side effects (unpublished data, details of which will be published elsewhere). It may be mentioned here that evening primrose oil contains about 70% LA, and 9% GLA and we believe that probably GLA is more active than LA in augmenting peptic ulcer healing, though this remains to be substantiated by further testing. Other PUFAs like eicosapentaenoic acid (EPA) may also have a role in peptic ulcer disease. Peptic ulcer is very rare in Eskimos⁶ whose diet is rich in EPA. It is interesting to note that EPA is known to compete with AA and displace it and inhibit synthesis of 2 series PGs.¹⁷ We have recently shown that both n-3 and n-6 PUFAs can kill tumour cells selectively and that this action is not dependent on their conversion to PGs.¹⁸-¹⁹

These evidences indicate that EFAs/PUFAs may have a more direct role in peptic ulcer disease and other conditions and that their conversion to PGs may not always be necessary to bring about their actions.

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