Gastric luminal epidermal growth factor is affected by diet

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Objective. Diet is an area of major interest to those investigating the causes of cancer of the oesophagus in the Transkei. This study looked at the associations between intragastric epidermal growth factor level, diet and intragastric pH.

Setting and subjects. A dietary survey was co-ordinated with studies of gastric luminal epidermal growth factor and gastric fluid pH in 120 rural Transkeians.

Results. Gastric fluid epidermal growth factor was associated with low dietary intake of animal products ($p = 0.002$) and vegetables ($p = 0.026$). There was no association with pH.

Conclusion. A dietary subgroup has been identified in the Transkei population with high levels of epidermal growth factor in the upper gastrointestinal lumen. This adds to previously demonstrated diet-related changes in the upper gastrointestinal tract in Transkei. These changes may affect the disease pattern of the population.

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Diet has long been a major area of interest to those investigating the causes of endemic squamous cancer of the oesophagus in the Transkei. In South Africa, suspicion has been cast on general deficiencies,[1] specific deficiencies,[2] specific dietary content, e.g. alcohol[3] and *Solanum nigrum*, a wild vegetable,[4] and on contaminants in the diet such as fumonisins.[5]

The first part of this study of diet and gastric fluid, published last year,[6] showed that pH in a rural Transkei population was biphasic and related to diet, most strongly to intake of maize. This second part of the study looked at the associations between diet, pH and levels of epidermal growth factor (EGF) in the stomach. EGF is a small polypeptide and one of the main gastrointestinal mitogens. In the gastric lumen it normally has a short half-life of 1.4 minutes.[7] It is cleaved in acid/pepsin to less active forms that are 3 - 4 times less potent; however, very little EGF is cleaved if the pH is above 4.[8]

Patients and methods

Ethical permission was obtained from the Ethics Committee of the Faculty of Health Sciences, University of Transkei. One hundred and twenty volunteers were recruited from among patients attending a rural health clinic, and informed consent was obtained. Patients who were smokers, who had symptoms of upper gastrointestinal disease, or who were receiving non-steroidal anti-inflammatory drugs were excluded from the study.

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A food frequency questionnaire was used which included 23 items identified as the most frequently eaten foods in rural Transkei (Fig. 1). These included 5 broad categories, viz. maize-based foods, animal products, fats and oils, fruit, and vegetables.

Consumption was recorded as daily, several times per week, weekly, monthly, yearly or never. For statistical calculations, 'several times per week' was assumed to be 3 times per week.

Gastric juice was obtained from each volunteer, after an overnight fast, using a fine-bore nasogastric tube. The fluid obtained was transported in liquid nitrogen, and stored at –40°C before analysis. The pH was measured by glass electrode. EGF was measured using an enzyme-linked

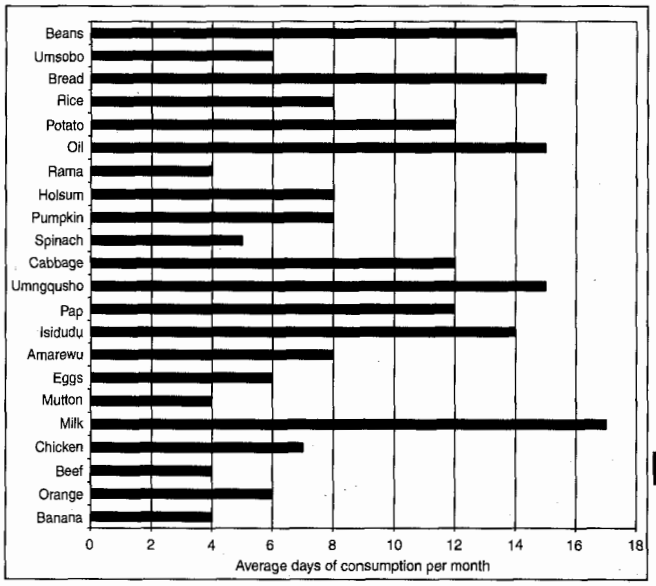

Fig. 1. Frequency of consumption of various foods in volunteers (umsobo — Solanum nigrum; umngqusko — stamped maize; amarewu — fermented maize drink).

immunosorbent assay (ELISA) (R and D Systems, Minneapolis, Minn., USA, #DEGOO).

The relationships between individual dietary components, EGF and pH were studied using Spearman's rank correlation, and SPSS software (Chicago, Ill., USA).

Results

Results were available for all patients (Fig. 1). Gastric fluid EGF was associated with low dietary intake of foods of animal origin ($p = 0.002$) and vegetables ($p = 0.026$) (Figs 2 and 3). There was a non-significant association with low total fat intake ($p = 0.076$), but no significant association with any individual food. There was no association with intragastric pH (Table I).

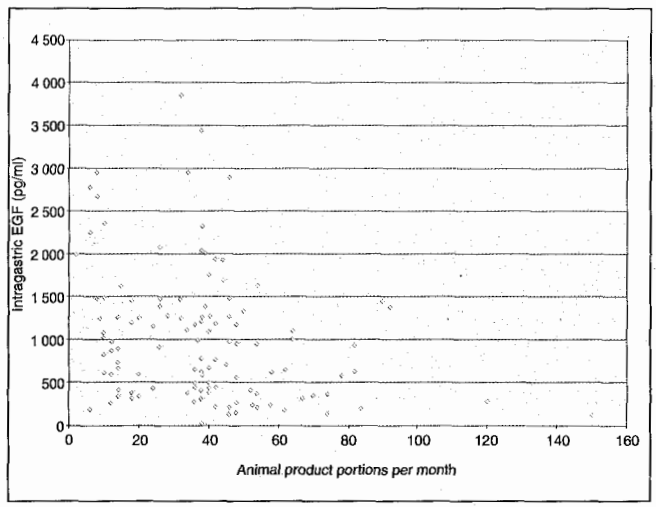

Fig. 2. Animal product consumption and intragastric EGF.

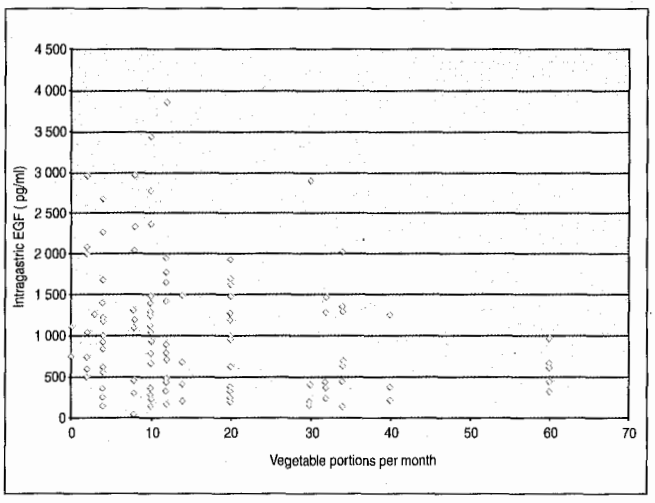

Fig. 3. Vegetable consumption and intragastric EGF.

Table I. Associations between foods consumed, intragastric pH and intragastric EGF

	Spearman's correlation coefficient	Significance (2-tailed)
Individual foods	No significant associations	
Food groups		
Fruit	0.012	0.894
Animal products	–0.283	0.002
Maize	–0.129	0.158
Vegetables	–0.202	0.026
Fats	–0.162	0.076
pH	0.056	0.540

Discussion

The radioimmunoassay method used in this study does not distinguish between the different forms of EGF, and so the molecular levels detected do not equate accurately to EGF activity.

EGF is very labile, for instance rising to 10 times basal value in response to histamine stimulation.[9] This may explain why the literature is not clear on what constitutes a 'normal' gastric luminal EGF level. Several studies[10-12] support a level between 300 and 600 pg/ml, while other studies[9] support a level nearly 10 times higher than this.

In this study it would be reasonable to think that 'normal' included those on a broad-based diet with a good intake of protein, fruit and vegetables. EGF levels in such individuals were mostly below 1 000 pg/ml. 'Abnormal' may have included individuals with low protein and vegetable intake, with EGF levels over 1 000 pg/ml.

The strongest association in this study was with animal products – milk, chicken, mutton and beef. These all contain fat in addition to protein. These fats are significant in quantity and quality. It is worthy of note that other dietary fats may have had an effect on EGF since a non-significant difference was seen. Vegetable content includes vitamins and some fatty acids. On a marginal diet such as is eaten in Transkei the amounts of these substances derived from vegetables may be enough to influence EGF production or regulation.

With both meat and vegetables, the association shown might be spurious, and the true association may be with some other aspect of the adoption of a more westernised diet or way of life. The lack of association between EGF levels and fruit makes this explanation unlikely, since increased fruit consumption normally accompanies increased meat as part of a more westernised diet.

There was no association with pH levels. The first half of this study showed a strong association between maize intake and pH. It is of considerable interest that the diet of rural

Transkeians has now shown a second major diet-related phenomenon in the gastric lumen, not directly associated with the first.

The evidence presented suggests that there is a subsection of the population which has a high EGF, and in which that high EGF is not cleaved by pepsin activity. This subsection includes those who have a high intake of maize (and therefore a high intragastric pH), and a low consumption of animal products, vegetables and fats (and therefore a high EGF).

The group in South Africa susceptible to cancer of the oesophagus is poor but not very poor, and has a narrow diet highly dependent on maize, pumpkin and beans, and low in fats.[4,13] This susceptible group appears to be the same as the subsection of the population who have raised pH and EGF. There is a good theoretical basis for an aetiological link to cancer of the oesophagus.[14] EGF is known to be a powerful mitogen.[15] It has been suggested that it may function as a co-carcinogen because of its mitogenic drive.[16] EGF has also been shown as a promoter of established squamous cancer.[17] Overexpression of transforming growth factor (TGF)-alpha, EGF and epidermal growth factor receptor (EGFR) is closely correlated with tumour invasion and prognosis.[18]

The subsection of the Transkeian population with a high pH and EGF will have a strong mitogenic, possibly mutagenic drive from EGF activity.

Statistical analysis was carried out by Mr Chris Foy, medical statistician, Research and Development Support Unit, Gloucestershire, UK.

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