Dr. P. J. van Eeden, Dept of Internal Medicine, University of Stellenbosch, high risk patient who is prone to develop enteric reflux after duodenal ulcer surgery (abstract).

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Gastric juice carcino-embryonic antigen estimation

A useful additional test in the diagnosis of gastric carcinoma?

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Summary

There is a high incidence of gastric carcinoma in the coloured population of the Western Cape. Diagnostic tests other than barium meal examination or gastroscopy were investigated. In this study 50 patients were assessed and grouped according to the gastroscopic and histological findings. Twenty-five patients with gastric carcinoma and 25 with benign gastric ulcer and/or chronic atrophic gastritis and/or intestinal metaplasia were tabulated. The gastric juice and plasma carcino-embryonic antigen (CEA) levels were measured and compared in the two groups. The gastric juice CEA level was more useful than the plasma CEA level as an aid in diagnosing malignant gastric lesions.

No correlation was evident between CEA values and the extent of the gastric carcinoma and or histological typing. An elevated gastric juice CEA level was an additional aid in diagnosing gastric carcinoma. Markedly elevated values may also identify the high-risk patient who is prone to develop gastric carcinoma.

The highest incidence of gastric carcinoma in South Africa and the fourth-highest incidence in the world are attributed to coloured males living in the Western Cape. These patients present at an advanced stage of the disease and 40 - 60% of cases are not amenable to surgical resection. Earlier diagnosis would be desirable for a surgical cure or longer postoperative survival. Diagnosis of gastric carcinoma could be made earlier by: (i) using tests other than histological examination to distinguish benign from malignant lesions; and (ii) identifying the high-risk patient and subjecting him to regular follow-up studies.

Carcino-embryonic antigen (CEA) has been utilised as an aid in the diagnosis of gastric carcinoma by several workers. CEA is a glycoprotein with antigenic properties. High CEA values are usually evident in the fetal gastro-intestinal tract at 2 - 6 months, and its level is abnormally elevated in adults with malignant gastro-intestinal lesions. CEA is at present utilised not only in the diagnosis of malignant gastro-intestinal disease but also as a test after surgery to detect recurrence.

References:
CEA is excreted in body fluids such as the gastric juice. No literature is available on the subject in South African population groups, and we therefore estimated CEA values in the serum and gastric juice of gastric carcinoma patients.

The purpose of this study was to determine whether: (i) CEA estimations in gastric juice are of greater value than in plasma for the diagnosis of gastric disease; (ii) gastric juice CEA values would be useful as an additional diagnostic aid in gastric carcinoma; and (iii) the diagnostic value of gastric juice CEA determinations in the detection of gastric carcinoma could be improved.

Patients and methods

Fifty patients underwent clinical, radiological and endoscopic evaluation in the Gastro-intestinal Clinic at Tygerberg Hospital. These patients were separated in order of their referral to the clinic into a gastric carcinoma and a control group.

Group I (gastric carcinoma group) consisted of 25 patients with macroscopic and histologically proven gastric carcinoma. Group II (control group) consisted of 25 patients with histologically proven benign gastric ulcers and/or intestinal metaplasia and/or chronic atrophic gastritis. Fasting gastric juice samples were obtained during gastroscopy or with a nasogastric tube. Macroscopically bloody or contaminated samples were discarded. A fasting blood specimen was obtained at the same time.

Centrifuged supernatant gastric juice and serum were stored at −40°C until sufficient samples were ready for CEA estimations. A 1:50 dilution of gastric juice was used and CEA was estimated by the Phadebas CEA Prist method based on the radio-immunoassay method for the determination of IgE.11–14 No correction was made for the protein content of the gastric juice.

Results

The median age of patients in the gastric carcinoma group was 57 years (range 19 - 79 years) and that of patients in the control group 54 years (range 29 - 76 years). The majority of the patients (80%) were coloureds; 16% were white and 4% black.

The gastric carcinoma group included the following histological types: (i) well differentiated (2 cases); (ii) moderately differentiated (4); (iii) poorly differentiated (12); (iv) undifferentiated (2); (v) signet-ring carcinoma (5).

In accordance with the TNM (tumour, node, metastasis) classification 8 patients were in classes T2 and T3 and 17 in T4. Final TNM classification could not be obtained for 14 patients not operated upon.

In the control group endoscopy revealed 17 cases of macroscopically benign gastric ulcer and, 12 of gastritis (4 patients had a benign ulcer and gastritis). The control group included the following histological types: (i) acute or subacute gastric ulcer and fibrinopurulent exudate on biopsy (13 cases); (ii) chronic atrophic gastritis (5); and (iii) intestinal metaplasia (5) — in 6 cases (3 of small benign gastric ulcerations and 3 of macroscopic chronic gastritis) no histological opinion was obtained. Some of the patients had lesions of more than one histological type.

The plasma CEA values are presented in Fig. 1 and the gastric juice CEA values in Fig. 2. Plasma CEA levels could be measured within the range of 2.5 - 250 µg/l. If the values were above 250 µg/l the serum was further diluted. Plasma CEA levels of less than 7.5 µg/l for smokers and less than 5.0 µg/l for non-smokers were considered normal. Plasma CEA values were abnormal in 44% of the gastric carcinoma group, in comparison with 28% of the control group. The median plasma value in the gastric carcinoma group was 8,0 µg/l compared with 4,6 µg/l in the control group.

If the upper limit of normal for gastric juice CEA can be taken as 25 µg/l, then positive results were obtained for all the patients with gastric carcinoma and for 76% of those in the control group.

These values are presented in Table I.

It is evident that gastric juice CEA estimation gives a very good indication of gastric carcinoma but is not specifically diagnostic.

![Fig. 1. Plasma CEA values.](image)

![Fig. 2. Gastric juice CEA values.](image)

The median gastric juice values were 1500 µg/l in the gastric carcinoma group, in contrast to 150 µg/l in the benign gastric ulcer group. No correlation was found with the correlation matrix test among the four different subgroups of CEA values (plasma and gastric CEA values in the gastric carcinoma and control groups). The Spearman rank test showed some correlation between plasma and gastric juice CEA values in the gastric carcinoma group (r = 0,502; P < 0,05).
Comparing the gastric carcinoma and control groups, plasma CEA as well as gastric juice CEA values were significantly different (Mann-Whitney U-test, \( P < 0.01 \) and \( P < 0.0001 \) respectively).

No correlation could be found between the TNM classification or tumour size and CEA values, or between the different histological types of gastric carcinoma and the CEA values. The control group was histologically classified into acute, subacute and chronic atrophic gastritis and intestinal metaplasia. There was no correlation between the different benign histological types in this control group and the CEA value. The subgroups are, however, too small to expect any statistically meaningful difference.

**Discussion**

At our clinic it is often a problem to differentiate a benign gastric ulcer from a gastric carcinoma. In spite of radiological, gastroscopic and histological investigations it is not always possible to confirm or to disprove gastric carcinoma with certainty before operation. An average of about 50 patients with symptomatic gastric carcinoma are diagnosed annually at our clinic. These 50 patients represent about 61% of the total number of patients referred to us with an initial diagnosis of gastric carcinoma.\(^{10}\)

The two groups of patients in this study may not be entirely comparable; factors such as age and sex may play a role in small groups of 25 patients each. In this study, however, gastric juice CEA estimation was of greater value than plasma CEA estimation in differentiating gastric diseases. Previous workers have rarely found an increase in gastric juice CEA values in the absence of any gastro-intestinal lesion.\(^3\) Raised gastric juice CEA values are, however, not diagnostic of gastric carcinoma.

Upper limits of normal of 25 \( \mu g/l \) or 100 \( \mu g/l \) have previously been accepted,\(^4\) but this limit should be increased to more than 1000 \( \mu g/l \) to improve the diagnostic value of gastric juice CEA estimations in gastric carcinoma. If the gastric juice CEA value is greater than 1000 \( \mu g/l \), the patient has a 60% chance of having gastric carcinoma; if it is less than 100 \( \mu g/l \), the patient only has an 8% chance.

Our estimations were not corrected for the protein content of the gastric juice to compensate for sampling error. Uncorrected gastric juice CEA estimations are, however, still valid in detecting the high-risk patient and in planning treatment or follow-up. The value of follow-up with gastroscopy, serial biopsies and gastric juice CEA estimations will be studied in a future survey.

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**REFERENCES**